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The October cover photographer of "Indigo Bunting" contact information: Fred Baker, fbdesign1@ verizon.net, phone (401) 788-0111.

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COMMENTARIES

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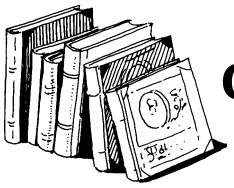

Commentaries

Rat Doctors

A world renowned expert, chair of a neurology department at a prestigious university, gave an invited talk at an international congress, talking about his field of expertise, pathophysiology of brainstem function in animal models of a behavior seen in **Parkinson's disease (PD).** He was asked a question about the actual human condition: If the region of the brain he discussed was so impaired in every PD patient, why wasn't that clinical problem seen more? The expert noted that if one was clever enough to ask the correct questions and delve into the issue adequately, it was far more common than the literature would suggest and was virtually ubiquitous.

That comment provoked this column. I have been interested in the behavior under discussion and have, in fact, delved into the question. I am familiar with the clinical literature, which clearly shows that the problem affects under 30% of PD patients, whether one uses intensive questionnaires or laboratory testing, one of which is the "gold standard" depending on who you are. I have probably seen over 100 times as many PD patients as the expert, and the 30% estimate is probably correct. And since I've contributed a few papers to the clinical literature, including data from first hand observation, I think I have a reasonable handle on the problem.

As they say in the trade, "If you don't know the answer, then baffle them with baloney."

I worry about the impact observations by such researchers make on people who are not experts in the field. I understand why the expert feels the need to extend his aura from the laboratory to the clinic. He wants to be perceived as the omni-competent, omniscient ubermensch who deserves his distinguished position. He needs to show that he is not simply a lab expert. He *understands* the disorder based on animal and human experience. It is hard to understand, however, how one can be a clinical expert when one sees patients one half day each week (when not traveling to a conference or too busy to attend the clinic). This isn't to say there aren't such people. I have met them and stand in awe of them. There aren't too many of them. however, and far fewer than they think.

I am familiar with prestigious institutions which have a myriad of experts in my field of movement disorders who each see patients one half day per week. For some reason there is a feeling that laboratory experts have expertise in clinical medicine whereas clinical experts never think their competence extends into the laboratory. The latter is understandable; the former, less so.

The danger lies in the impact an "expert" may make on an unwitting listener who cannot distinguish between the "rat doctor's*" expertise and the clinician expert. The "rat doctor," who may be world famous, is famous for his laboratory observations. He should limit his expert comments to this area in which he is, in fact, expert. He should speculate on what his observations mean in "the real world," meaning, the world of human patients. His basic research work is always focused on this, the ultimate goal of all medical research. This work is the beginning of the translational research road. The problem arises when the doctor confuses his white coat, medical degree and animal research contributions with clinical knowledge.

I heard a wonderful joke from a neurosurgeon. When a doctor has seen one case, he talks about his experience. When he's seen two cases he describes his "series." When he's seen three cases, it becomes, "In case after case after case…" So when the rat doctor reports that a problem affects 75% of his cases whereas studies report less than 30%, one wonders if this represents three of four cases or 75 out of a 100; how did he interview these patients; how did these patients get to see him in the first place?

Another neurology chair asked his movement disorders chief, an internationally recognized figure, whom he would see if he had PD and lived in a city where there was a world renowned researcher and a locally-well known PD clinician who had written books for patients. When the PD expert said there was no question that he'd see the clinical expert the chair was astounded. "But so and so is a first rate scientist and very famous! The other guy doesn't even publish."

At a meeting of one of the state PD support associations a motivational speaker taught patients that the abbreviation, MD, stands for medical doctor not "medical deity." She said, "Listen to your doctor, but he's not god, no matter what he thinks." An RN told me that at a lecture she gave to PD nurses she tried to make the point over and over that the RNs had to worry less about what their physician supervisors think about them and do more to support their patients, even if it meant a confrontation with the MD. I responded that it was too bad that more doctors didn't worry about what people thought about them, less about being paragons of knowledge and competence.

Who knows what we look like to our patients, staff, colleagues or students? Gazing at ourselves in the mirror isn't enough. After all, look what happened to Narcissus.

– Joseph H. Friedman, MD

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* I am obliged to Brian Ott, MD, who learned the term "rat doctor" from one of his clinical mentors, who was not laboratory based, and passed it on to me.

The Tenacity of Tuberculosis

Tuberculosis [TB], paleontologists tell us, has been with us since prehistoric antiquity, a conclusion based upon their demonstration that the fossil bones of some of our ancient ancestors show the distinctive stigmata of TB. Nor, in recent centuries, has TB been a rare or exotic affliction. Indeed, many medical demographers claim that TB, through the last millenium, has affected more humans, and killed more, than any other known contagious agent.

Many of the infectious diseases that have burdened mankind historically seem to have arisen in a defined geographic site and then, belatedly, spread to the remainder of the globe. Cholera, for example, confined itself to the Ganges delta for centuries until aggressive colonialism within and beyond the eastern Indian subcontinent accelerated its 19th Century global spread (arriving in this nation by 1831).. The same has been true of such initially regional diseases such as bubonic plague, measles, influenza and smallpox. TB, in contrast, has surfaced in virtually all geographic regions, in all cultures and in all of the many centuries of recorded history. If TB had once been localized to a specific geographic site – a likely event – that site has yet to be demonstrated.

When confronting the problem and even the extent of TB, it is imperative to understand the unique interrelationships between the TB organisms and humans. The dynamics of clinically active TB can only be understood by first acknowledging the continued intimacy involving humans and TB germs.

For the sake of discussion, consider the world to be divided into four biologically discrete groups: Those humans with clinically active TB, usually involving the lungs; those individuals who had previously had active TB but are now cured; those who currently harbor a few TB germs sequestered in some internal lymph node but show no present sign of active TB; and finally, those who have yet to encounter the TB bacilli.

Three of these TB-related categories are self-evident; it is the third, those ostensibly healthy individuals who have hidden clusters of "sleeping" TB germs, that create epidemiologic nightmares. These TB germs may remain dormant for years, even decades. The World Health Organization estimates that one-third of the world, about two billion humans, are in this category. These are the vulnerable ones: When they are confronted by great physiologic stress, when undergoing extensive radiation therapy or when their immune system is suppressed [as in HIV infection] they then face the likelihood of TB activation.

The historic resurgence of TB in Europe coincided with the Industrial Revolution of the 17th and 18th Centuries as factory-type employment caused massive migration into the cities. The resulting urban overcrowding provided the ideal setting for the air-borne spread of the germs of TB. Other 18th Century social institutions such as the expanded prisons, work houses, orphan asylums and enclosures for the mentally deranged conjoined to make TB the leading cause of adult mortality.

TB followed the same pattern in this nation: New immigrants concentrated in the cities rather than the rural communities, lodging particularly in the overcrowded urban tenements where the spread of airborne disease was augmented by poor nutrition, poor air circulation in the slum dwellings and, in general, an environment of pervasive poverty.

Until recently, the United States could take pride in its gradual conquest of TB, what the Victorians had chosen to call the white plague. The development of better, healthier housing, the various aggressive public health measures to identify early TB and rapidly segregate its victims into institutions called sanatoria thus diminishing the major source of TB contagion. (The U.S. Public Health Service estimated that the average person with active TB infects about 20 other humans during his lifetime unless he is isolated during the active phase of his disease in a TB sanatorium.) These TB institutions, typically in rural settings, fulfilled a dual purpose: a quiet place for consumptives to heal; and a preventive measure to interrupt the customary paths of TB communicability. The incidence of TB then fell precipitously even before the introduction of streptomycin in the late 1940s, the first antibiotic agent capable of curing TB.

Toward the end of the 20th Century, however, the incidence rate of active, clinically apparent TB rose dramatically, in this nation. In the New York City borough of the Bronx, during the last decade of the 20th Century, public health officials were confronted with three critical problems enhancing the spread of TB: first, an increase in strains of TB now resistant to the customary antibiotic drugs; second, the crowded tenements of the region were becoming increasingly over-congested with newly arriving Caribbean and Asiatic immigrants; and third, an epidemic of HIV infection spreading rapidly within this inner city community. What was taking place in the Bronx was reproduced in numerous other impoverished enclaves of the United States.

The problem has not reached the level of national concern in this nation largely because the recrudescence of TB has been confined to our immigrant and poverty-stricken population. The rate of TB amongst established, middle-class communities remains at a very low level. And in the remainder of the world? Drug-resistant TB is now increasing dramatically in the new urban centers of South Africa, India and China coincident with their rampant industrialization. And wherever HIV infection has been implanted, as in sub-Saharan Africa, so too has TB returned to become a major public health threat. HIV and TB have now merged, in synergy, to create an evil confederacy.

– Stanley M. Aronson, MD

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Stanley M. Aronson, MD, has no financial interests to disclose.

Correspondence

e-mail: SMAMD@cox.net

AIDS-Related Lymphomas: The Rhode Island Experience

Jorge Castillo, MD, Caitlin Hansen, Anthony Mega, MD, Karen Tashima, MD

The majority of HIV-infected persons in Rhode Island receive care at the Samuel and Esther Chester Immunology Center located at The Miriam Hospital in Providence, Rhode Island. The Immunology Center provides HIV care for approximately 1100 patients. The Center provides multiple services onsite including free HIV counseling and testing (rapid blood and/or saliva testing), onsite counseling and social work, medical care, clinical trials, limited psychiatric care, viral hepatitis treatment, substance abuse referral system, and adherence nursing. In 2006, the average age of the Immunology Center patient was 44 years; 65% of patients were male and 35% female. Thirty-one percent had private medical insurance, 51% public insurance, and 19% were uninsured. Fifty-two percent have been diagnosed with AIDS and three quarters are taking highly active antiretroviral therapy, of whom 61% have achieved full viral suppression on therapy. Thirty-two percent have concomitant hepatitis C infection, and 5% have chronic hepatitis B infection.

According to the **Rhode Island Department of Health (HEALTH)**,[1] in 2006 there were 1,467 Rhode Islanders living with AIDS, mostly in greater Providence. Between 2000 and 2006, the percentage of women diagnosed with AIDS increased from 24% to 34%. People diagnosed with AIDS were more likely to be in the 40-49 year age group (39%) in 2006. Whites represented almost 43% of the new AIDS cases in 2006, African Americans 30%, and Hispanics represented 22% of new AIDS cases. Between 2000 and 2006, 981 individuals were diagnosed with HIV infection but did not have AIDS.

At this time, three conditions are considered AIDS-defining malignancies: B-cell **non-Hodgkin lymphoma (NHL)** of intermediate or high-grade histology, **Kaposi sarcoma (KS)** and invasive cervical cancer.[2] KS is the most common malignancy in HIV-affected individuals, but its incidence is decreasing secondary to the use of HAART. B-cell NHL is the second most common HIV-associated malignancy. In the absence of HAART, patients with HIV infection have 60 to 100 times increased risk of developing ARL when compared to the general population. Up to 90% of the ARL are **diffuse large B-cell lymphoma (DLBCL)** or **Burkitt/Burkitt-like lymphoma (BL/BLL)**. The risk of developing low-grade B-cell NHL, **Hodgkin disease (HD)** and T-cell NHL is also increased in HIV-infected patienta.[3,4] The **World Health Organization (WHO)** recently classified ARL in a comprehensive manner. (Table 1) ARL, with an incidence of 5% as an AIDS-defining illness, accounts for up to 23% of the mortality in patients infected with HIV.[5]

This report describes the experience of hospital-based Immunology clinic in regards to ARL epidemiology, diagnosis and management from 1996 to 2006.

Materials and Methods

Our primary objective is to describe the epidemiological, histological and clinical features of ARL in the post-HAART era. The population consisted of HIV-positive male and female patients of our Center, age 18 to 60, who were diagnosed with ARL from 1996 to 2006. The following diagnoses of lymphoma were included: B-cell NHL (DLBCL, BL/BLL, primary effusion lymphoma [PEL], and PCNSL), T-cell NHL and HD. Subject population was identified through direct physician communication and search of medical records database by the criteria listed above.

This report will include data on duration of HIV infection prior to diagnosis, most likely route of transmission of HIV, use of HAART, CD4 count and plasma HIV RNA levels on diagnosis, clinical features, histological type, staging and therapy used for ARL and final outcome. Our long-term objective was to add to the current body of knowledge of the clinical features and treatment of ARL, with particular attention to the impact of HAART.

Results

Twenty-two cases of ARL were diagnosed at our Institution. (Tables 2 and 3)

The median age at presentation was 43 years with a range of 28 to 60 years. Men predominated, 6.3:1. Patients had an average of 7.7 years, ranging from less than a year to 22 years, since the initial diagnosis of HIV infection. The most common HIV transmission route was male-to-male sexual contact (36%) followed by intravenous drug use (23%) and heterosexual contact (14%); other routes of transmission include transfusions, blood-borne and unknown (27%). The mean CD4 count at ARL presentation was 207 cells per cubic millimeter. Patients diagnosed with ARL had an average of 1.4 years since institution of HAART; all the patients were exposed to HAART at some point during their disease. At diagnosis, 50% of the patients were receiving HAART. From the patients who were not on HAART at the time of diagnosis, 64% started HAART during treatment, and 36% started HAART after the treatment for ARL was finished.

Table 1. WHO Classification of HIV-Associated Lymphomas

Lymphomas also occuring in immunocompetent patients
- Burkitt/Burkitt-like lymphoma
- Diffuse large B-cell lymphoma+
- Peripheral T-cell lymphoma
- Hodgkin lymphoma

Lymphomas occuring more specifically in patients who are HIV positive
- Primary effusion lymphoma*
- Plasmablastic lymphoma of the oral cavity*

Lymphomas occuring in other immunodeficiency states
- Polymorphic B-cell lymphoma

+ Includes primary CNS lymphoma * Subtypes of diffuse large B-cell lymphoma

Table 2. General characteristics of the subject population

Mean age in years (range)	43 (28-60)
Sex	
Male	19 (96.4%)
Female	3 (13.6%)
Mean duration of HIV infection in years (range)	7.7 (<1-22)
Most likely route of HIV transmission	
Male-to-male	8 (36.3%)
IV drug use	5 (22.7%)
Heterosexual	3 (13.6%)
Others/Unknown	6 (27.2%)
Mean CD4 count at presentation in cells/m m3 (n=21)	207
CD4 count for NHL (range)	165 (4-518)
CD4 count for HD (range)	337 (12-1155)
Mean duration of HAART in years (range)	1.4 (<1–9)
Institution of HAART	
Prior to ARL diagnosis	11 (50%)
During therapy for ARL	7 (31.8%)
After finishing therapy for ARL	4 (18.2%)

Table 3. ARL-associated characteristics of the subject population

Lymphoma type	
DLBCL	10 (45.5%)
BL/BLL	5 (22.7%)
NHL, NOS	1 (4.5%)
TCL	1 (4.5%)
HD	5 (22.7%)
ARL stage (n=10)	
I and II	3 (30%)
III and IV	7 (70%)
B symptoms	
Yes	14 (63.6%)
Lymphoma location	
Extranodal	11 (50%)
Nodal	11 (50%)
Therapy	
Chemotherapy	16 (72.7%)
Radiation therapy	2 (9.1%)
Multimodality	1 (4.5%)
Outcome	
Expired	6 (27.3%)
Alive	11 (50%)
Lost to follow-up	5 (22.7%)
Survival (months)	46 (0-139)
DLBCL	42
BL/BLL	24
HD	57

From the ARL standpoint, there were 15 cases of B-cell NHL; the most common histology was DLBCL (32%) followed by BL/BLL (23%); other histological types were also observed, such as PEL, PCNSL and unspecified NHL (18%). T-cell NHL was observed in one patient (5%) while HD was diagnosed in 5 patients (23%). More than 60% of the patients with ARL presented clinically with B symptoms (unexplained weight loss, fever or drenching night sweats) and 70% of them presented with Ann Arbor stages III or IV. As expected, 50% of the patients presented with extranodal disease affecting bone marrow, liver, CNS, stomach, jaw and nasal cavity.

Sixteen patients received chemotherapy, radiation therapy alone was used in 2 patients, one patient with PCNSL was treated with a multimodal approach (surgery followed by chemotherapy), and 3 patients had an unknown type of therapy. Patients diagnosed with NHL were treated with cytotoxic chemotherapy in 75% of the cases; the most commonly used regimens were CHOP (cyclophosphamide, daunorubicin, vincristine and prednisone) and EPOCH (etoposide, daunorubicin, vincristine, cyclophosphamide and prednisone). Rituximab, an anti-CD20 monoclonal antibody, was used in 3 cases; two cases received rituximab along with CHOP and one patient received rituximab as a single agent. Patients diagnosed with HD were treated with ABVD (daunorubicin, bleomycin, vinblastine and dacarbazine) in 80% of the cases; the remainder case received radiotherapy alone. The only case of T-cell NHL was treated with radiotherapy alone.

At the time of this report, 6 patients had died, 5 patients were lost to follow-up, and the remaining 11 were still alive; from the latter group, 73% were in remission. The overall survival was 46 months and the median survival of the patients who died was 36 months. Patients with DLBCL and HL had longer survival time than patients with BL/BLL (57 months, 42 months, and 24 months, respectively).

Discussion

ARL has been reported to affect mainly young HIV-positive male individuals; in our series the median age of presentation was 43 years old and there was a clear male predominance. The route of HIV transmission does not seem to play an important role in the incidence of these malignancies, but we have a small case series. As mentioned, ARL is the second most common malignancy observed in HIV-positive individuals. Antiretroviral therapy has become very effective in decreasing infectious complications and has decreased the incidence of KS;[6] although HAART has also shown to decrease the incidence of ARL,[7,8] it has done so to a lesser degree, hence the relative increase in the incidence of this malignancy in HIV patients.[6] Furthermore, the incidence of some types of lymphoma, such as BL/BLL, has not been greatly affected by the use of HAART.[9]

ARL may be observed in HIV patients either as an initial presentation, as in 6 patients from our series, or at any time during the course of their disease; in our report, one patient was diagnosed with ARL 22 years after his initial diagnosis of AIDS. Some types of ARL are more likely to be seen in patients with lower CD4 counts (PCNSL and DLBCL), while others are likely to develop in the presence of higher counts, like BL/BLL and HD.

The most common ARL subtype is aggressive B-cell NHL: it accounts for 80% to 90% of the cases. In our series, DLBCL and BL/BLL accounted for 70% of the cases. HIV-infected patients have an increased risk of developing other non-AIDS-defining lymphomas; the risk of developing TCL and HD has been reported increased 15-fold and 5 to 9-fold, respectively.[3,4] The pathogenesis of ARL is incompletely understood, but HIV seems to play an indirect role through immunodeficiency, cytokine deregulation of the microenvironment and chronic antigenic stimulation by HIV antigens. Functional and quantitative defects in T-cells and NK-cells are part of the many immune abnormalities induced by HIV. IL-6 and IL-10, which are produced inherently by HIV-infected cells, will promote a B-cell hyperactivation state.[10] This state of generalized hyperproliferation and immunosuppression favors EBV infections; EBV-infected immortalized clones posses a constitutional genetic instability that allows the development of genetic rearrangements (MYC gene activation is observed in 75% of B-cell ARL) permitting the development of malignant lymphoma.[10] Clinically, ARL tend to present with B symptoms and at advanced stages; involvement of the bone marrow and the CNS exemplifies the predilection of these lymphomas for extranodal sites.

The most extensive data regarding treatment exist for DLBCL. At this time, CHOP is the most commonly used regimen,[11] but EPOCH[12] and CDE (cyclophosphamide, doxorubicin and etoposide)[13] have achieved good response and survival rates. In this setting, CNS prophylaxis should be considered in patients with testicular, epidural, paranasal and bone marrow involvement. HIV-associated BL/BLL patients with good immune status (CD4 > 100 cells per mm3) have been treated with more intensive therapies with good response and survival.[14, 15] For those BL/BLL patients with lower CD4 counts, CHOP could be considered; CNS prophylaxis is mandatory in this setting but there is no clear consensus about the best regimen to use. For HIV-associated HD, regimens like ABVD[16] and BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone)[17] have been tried with success. In general terms, our patients with ARL are being treated more like their immunocompetent counterparts with better results, which are in part due to improved supportive care and better anti-infective therapies. All the previous regimens have been used along with HAART, growth factor support, and PCP and HSV prophylaxis using trimethoprim-sulfamethoxazole or pentamidine and acyclovir, respectively. Regarding HAART, most drugs have been used safely along with cytotoxic chemotherapy but zidovudine should be avoided given its bone marrow suppressing effects. The role of rituximab in combination with chemotherapy in the management of ARL is still debatable but it seems to be safer and beneficial in patients with CD4 counts higher than 100 cells per mm3.[18-20]

Conclusions

ARL is likely to affect patients in their early forties who have CD4 counts less than 200 cells per mm3. ARL can develop at any time during HIV infection and no environmental factor seems to play an important role in its development. A better understanding of the multiple pathogenetic mechanisms for the development of ARL is needed to improve the current therapeutic approaches. The patients in our series responded well to standard chemotherapeutic regimens despite their HIV status. Early use of HAART, G-CSF and prophylactic antibiotics appear to have eased the management of these malignancies. ARL patients are likely to benefit from rituximab, although its role needs to be further elucidated.

The data from the Miriam Hospital Immunology Clinic for the last 10 years is similar to that reported from other parts of the developed world. Infections are still the most common AIDS-defining illnesses but because highly effective antiretroviral therapy improves the long-term outlook for patients infected with HIV, the incidence of malignancies, particularly ARL, may be increasing.

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Jorge Castillo, MD, is Assistant Professor of Medicine.

Caitlin Hansen is a medical student.

Anthony Mega, MD, is Assistant Professor of Medicine.

Karen Tashima, MD, is Assistant Professor of Medicine.

All are at the Warren Alpert Medical School of Brown University.

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Off-label use of medication: Rituximab has not been approved for AIDS lymphomas.

Correspondence:

Jorge Castillo, MD
Miriam Hospital
164 Summit Ave
Providence, RI 02906
e-mail: jcastillo@lifespan.org

Management of Behavioral Problems In Dementia

Robert Kohn, MD, MPhil, and G. Mustafa Surti, MD

Behavioral problems are common in dementia: up to 80% to 90% of patients develop at least one distressing symptom during the course of their illness.[1] A common descriptor to describe many of these symptoms is " agitation" (inappropriate verbal, vocal, or motor activity that is not judged by an outside observer to result directly from the needs or confusion of the individual).[2] Cohen-Mansfield has described four types of agitated behavior 1) verbally non-aggressive, e.g., complaining, negativism, repetitive sentences or questions, constant unwarranted requests for help; 2) verbally aggressive, e.g., screaming, verbal sexual advances or remarks, making strange noises, cursing; 3) physically non-aggressive, e.g., performing repetitious mannerisms, inappropriate dressing and disrobing, eating inappropriate substances, handling things inappropriately, trying to get to a different place, pacing, aimless wandering, moving furniture and things around, intentional falling, general restlessness, hoarding things, hiding things; and 4) physically aggressive, e.g., sexual advances, hurting self and others, throwing things, scratching, grabbing, pushing, kicking, biting hitting.[2]

Explanatory Models of Behavioral Problems in Dementia

Why do individuals with dementia develop behavioral problems?[3] The organic deterioration and the pathophysiological changes that ensue in dementia may directly result in behavioral changes. This is the Direct Impact Model.

Three other alternative explanatory models have been posited in addition to the Direct Impact Model. The Unmet Needs Model suggests that dementia results in a decreased ability to meet one's needs due to a deceased ability to communicate. These may include the patient's physical, emotional, environmental and social needs. The needs may include pain or other physical discomfort; mental discomfort such as depression and anxiety, lack of social contacts, an uncomfortable environment, or too little, too much or inappropriate stimulation. These needs may predate or develop following the onset of dementia. The Behavioral Model is based on the premise that its antecedents and consequences control problem behaviors. Patients learn problem behaviors through reinforcement by staff members or caregivers when a behavior is displayed. For example, reinforcement occurs when staff give an agitated patient increased attention. The final model is the Environmental Vulnerability Model. Dementia results in greater vulnerability to the environment; there is a lower threshold at which stimuli affects behavior. This Model suggests that a stimulus that may be appropriate for a cognitively intact person might result in an overreaction in a cognitively impaired person.

Instruments to Evaluate Behavioral Disturbance in Dementia

A number of scales examine behavioral disturbances in dementia. The most widely used scale is the Cohen-Mansfield Agitation Inventory, a 29-item scale that examines a range of physically aggressive, physically non-aggressive, and verbally agitated behavior from never to several times per hour on a seven-point scale.[4] In a shorter version, the Brief Agitation Rating Scale,[5] 10 items account for 90% of the variance of the Cohen-Mansfield Agitation Inventory and may be an adequate screening tool in nursing home settings. The Pittsburgh Agitation Scale is also a brief screening instrument; however, unlike the Cohen-Mansfield Agitation Inventory and the Brief Agitation Rating Scale it measure the severity and not the frequency of agitation.[6] The Pittsburgh Agitation Scale examines four groups of behaviors: aberrant vocalization, motor agitation, aggressiveness, and resisting care. The 25-item **Behavioral Pathology in Alzheimer's Disease rating scale** (**BEHAVE-AD**) , based on a four-point scale, explores the presence of paranoid and delusional ideations; hallucinations; activity disturbances; aggressivity; diurnal rhythm disturbance; affective disturbances; anxiety and phobias; and global rating of distress and dangerousness.[7] In psychopharmacological studies, the most widely used instrument is the Neurospsychiatric Inventory, which measures the frequency, the severity, and distress created around behavioral disturbances.[8] A nursing home version of the Neurospsychiatric Inventory taps domains that include delusions, hallucinations, agitation and aggression, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability and lability, aberrant motor behavior, nighttime behavior, and appetite changes. Other useful scales include: Overt Aggression Scale,[9] Overt Agitation Scale,[10] CERAD Behavior Rating Scale for Dementia,[11] and Caretaker Obstreperous-Behavior Rating Assessment.[12]

Differential Diagnosis of Behavioral Disturbance in Dementia

The differential diagnosis includes ruling out delirium. Common causes of delirium include urinary tract infections; electrolyte imbalance; dehydration; hypoglycemia; hypoxia; and drug toxicity. Laboratory studies including an urinalysis may be indicated. Some of the more common drugs that can lead to delirium in patients with dementia include anticholinergics, sedative hypnotics, narcotics, and steroids. Of note, anticholinergics also may lead to progression of dementia. A careful medication review should be conducted.

The presence of depression, anxiety and psychosis also need to be evaluated. Delusions are seen in 10% – 73% of individuals with dementia, primarily characterized by delusions of theft, suspiciousness, and threats of bodily harm.[13] Delusions of misidentification have been reported in about 25% of individuals with dementia. Hallucinations are estimated to occur from 21% to 49% in individuals with dementia;

visual are more common than auditory ones.

Other syndromes that need to be considered in the differential diagnosis include sundowning, caused by darkness. This is not delirium. It is hypothesized that it is due to alterations of the circadian rhythms and sensory inputs. The Catastrophic Reaction is brought on by environmental or psychological stress, often related to caregiver's behavior, such as being impatient, frequently changing the environment, blaming the individual with dementia, and giving complicated orders.

In trying to evaluate the etiology of the behavioral disturbance and to determine the treatment, the clinician should ask thirteen key questions:

What is the behavior?

- Under what circumstances or environment did the behavior occur?
- How often has the behavior occurred?
- How long did the behavioral problem last?
- How intense was the behavioral problem?
- What preceded the behavioral disturbance?
- Was the behavioral problem associated with daily activities?
- Does the patient have any control over the behavior?
- Does the behavioral problem occur when a specific person is present?
- How many people are present when the behavior occurs?
- What type of interactions is associated with the behavioral disturbance?
- What events predicted the behavioral disturbance?
- What function does the behavioral disturbance serve?

In addition, the clinician should investigate the presence of a premorbid psychiatric history. The behavioral problem may be a reflection of long-standing psychiatric issues and not necessarily an expression of new behaviors due to dementia. Premorbid psychiatric problems may have gone untreated; therefore, it may be useful to know: Was the patient always nervous? always difficult? Did the patient have a history of domestic violence? Did s/he drink too much or use drugs?

Pharmacological Treatment of Behavioral Disturbance in Dementia

Treatment of behavioral disturbance requires consideration of age and both pharmacological and non-pharmacological approaches. The pharmacological interventions should target as much as possible the etiology of the disturbance. If delirium is present then addressing the cause, such as using antibiotics to treat an underlying infection, may suffice. Depression in dementia is addressed by using antidepressants. **Selective serotonin reuptake inhibitors (SSRI)** are often considered the first line of treatment. Shorter-acting agents that have few drug-drug interactions are preferred, such as citalpram, escitalopram, and sertraline. Second line agents are the **neuradrenergic serotonin reuptake inhibitors (NSRI)**, which include venlafaxine and duloxetine. The former should be monitored for hypertension; the latter should be given with food due to nausea. Anticholinergic agents such as paroxetine and the tricyclics, e.g. amitryptyline and nortipyline, should be avoided. Bupropion may lower the seizure threshold and may be activating. Some nursing homes psychiatrists have used selegiline tansdermal, a monoamine oxidase inhibitor, in patients who won't cooperate with oral agents. Fluoxetine long-acting form given once a week is available. Mirtapine has been useful in depressed patients who have poor appetites or do not sleep well. The Alzheimer's drugs, the acetylcholinesterase inhibitors and memantine, have been shown to reduce depressive symptoms and should be considered an adjunct or even a first line treatment in mild cases. At times individuals with dementia and depression fail to respond to pharmacological interventions. Electroconvulsive therapy may prove beneficial in these situations.[14] A number of case reports have shown benefit in selected individuals whose behavior was characterized as screaming.[15]

The treatment of psychosis is controversial. First, there is a black box warning for antipsychotics as a class regarding their use in individuals with dementia regarding the potential for increased cebrovascular events and early mortality. Secondly, the CATIE-AD study suggested that there was little benefit in using antipsychotics in dementia psychosis compared to placebo.[16,17] Many antipscyhotics can cause weight gain, metabolic syndrome, and drug-induced Parkinsonism. Furthermore, elderly individuals are at increased risk for tardive dyskinesia. This is not to say that antipsychotics should not be used, as they are effective for many individuals. However, they should be used cautiously after the risks and benefits have been carefully weighed, and informed consent obtained. If an antipsychotic is used once the patient is stabilized, the clinician should consider tapering and discontinuing the pharmacological agent after 2 to 8 months of therapy. Response with an antipsychotic may occur with small dosages in patients who are not chronically mentally ill. Unfortunately divalpoex sodium, an alternative to antipsychotics, in placebo-controlled trials for agitation in Alzheimer's disease have been negative. One alternative to antipsychotics, in particular if the symptoms are mild, are acetylcholinesterase inhibitors and memantine.

Prior to using an antipsychotic in dementia the clinicinan should ask the following questions:

- Is the patient distressed by the psychotic symptoms?
- Whom are we treating the staff, caregiver, or patient?
- Is the behavior disruptive to other residents?
- Will the behavior result in loss of placement?
- Are there non-pharmacological interventions that can be tried?

Bipolar disorder at times also requires the use of antipsychotics; however, the same caution as with psychosis applies. Lithium, lomotragine, divalpoex sodium, carbemazapine and oxcarbazepine are all appropriate considerations. It has been suggested that lithium may have neuroprotective effects in dementia.[18] Lithium must be closely monitored for

toxicity due to reduced renal function with age.

In managing anxiety in dementia, as in depression and psychosis, consideration should be made for using acetylcholinesterase inhibitors or memantine. SSRIs are anxiolytic. Trazodone also may prove beneficial, and can be administered in small dosages several times during the day. Benzodiazipines, although not a fist line choice, may be necessary. If a benzodiazipine is to be used, consider using shorter acting agents, such as lorazepam. Any patient on a benzodiazepine should be closely monitored for fall risk and confusion. Quetiapine has been used increasingly among patients with dementia and behavioral disturbance. In particular, it has been used in divided dosages with small amounts before the behavioral problem usually begins and a larger does at bedtime. Although it may help some patients, this is not an indicated use; and the risks and cautions are similar to other antipsychotics.

Sleep disturbance is common among behaviorally disturbed patients with dementia. The first step in managing sleep is to treat the underlying problem. Light therapy may be beneficial especially in decreasing sundowning. The choice of medications to induce sleep should take into consideration those that are least likely to cause cognitive disturbance upon wakening. Ramelteon, a selective melantonin receptor agonist, appears safe, with little or no psychomotor or cognitive effects in the elderly. Two agents that are not indicated for sleep are frequently used in individuals with dementia: trazodone and mirtazapine. Zaleplon and eszopiclone are considerations if alternatives have failed; however, there is debate as to whether these agents have any advantage over benzodiazepines.

Non-Pharmacological Treatment of Behavioral Disturbance in Dementia

Non-pharmacological interventions are equally, if not even sometimes, more important than pharmacological interventions in managing behavioral disturbances in dementia. Most interventions are based on three of the models that lead to behavioral problems in dementia: interventions designed to address unmet needs; that are behavior and learning interventions such as caregiver interventions; and environmental interventions to reduce the stress threshold. A recent meta-analysis concluded that non-pharmacological interventions may be beneficial, including bright lights.[19] These conclusions, however, were based on only a few well-designed studies.

Non-pharmacological interventions should be the first step in behavior system management.

Several simple behavioral interventions can be readily implemented:[1]

- Correct sensory deficits; replace poorly fitting hearing aids, eyeglasses, and dentures
- Keep the environment calm, comfortable, and homelike with familiar possessions
- Provide regular daily activities and structure; refer patient to adult day care programs, if needed
- Attend to patient's sleep and eating patterns
- Install safety measures to prevent accidents
- Ensure that the caregiver has adequate respite
- Educate caregivers about practical aspects of dementia care
- Teach caregivers the skills of caregiving: communication skills, avoiding confrontational behavior management, techniques of ADL support, activities for dementia care
- Simplify bathing and dressing with adaptive clothing and assistive devices
- Provide access to experienced professionals and community resources
- Refer family and patient to local Alzheimer's Association

Conclusion

Behavior problems are one of the common causes of dementia requiring a physician's attention and/or hospitalization. The causes are frequently multifactoral; therefore, the management of the problem is also multifaceted.

Non-pharmacological interventions should be the first step in behavior system management. Later pharmacologic intervention should be tried if non-pharmacologic interventions are not sufficient. A multidisciplinary approach should be initiated, as the causes of behavioral problems are a combination of organic, behavior, environmental and psychological causes. Better behavior management is not only beneficial for the patient, but may lead to minimal environmental change and less stress on caregivers. Once a differential diagnosis has been obtained, a history of the behavioral problem elicited, and a work up conducted, both pharmacological and non-pharmacological interventions are important for behavior management, with the latter always being the first step.

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Robert Kohn, MD, MPhil, is Associate Professor of Psychiatry and Human Behavior, the Warren Alpert Medical School of Brown University; and Training Director of the Brown University Geriatric Psychiatry Fellowship Training Program.

G. Mustafa Surti, MD, is Clinical Assistant Professor of Psychiatry and Human Behavior, the Warren Alpert Medical School of Brown University.

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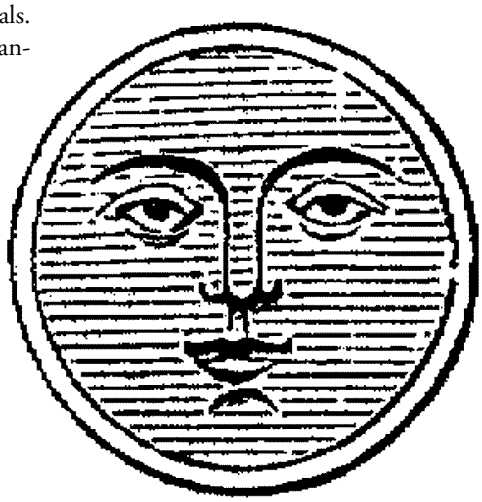
Discussion of off-label use of medications: All medication discussions are off-label; none are indicated for dementia.

CORRESPONDENCE:
Robert Kohn, MD, MPhil
Butler Hospital
345 Blackstone Blvd.
Providence, RI 02906
Phone: (401) 455-6277
e-mail: Robert_Kohn@brown.edu



Variations In Laboratory Testing During Medical Clearance of Psychiatric Patients In the Emergency Department

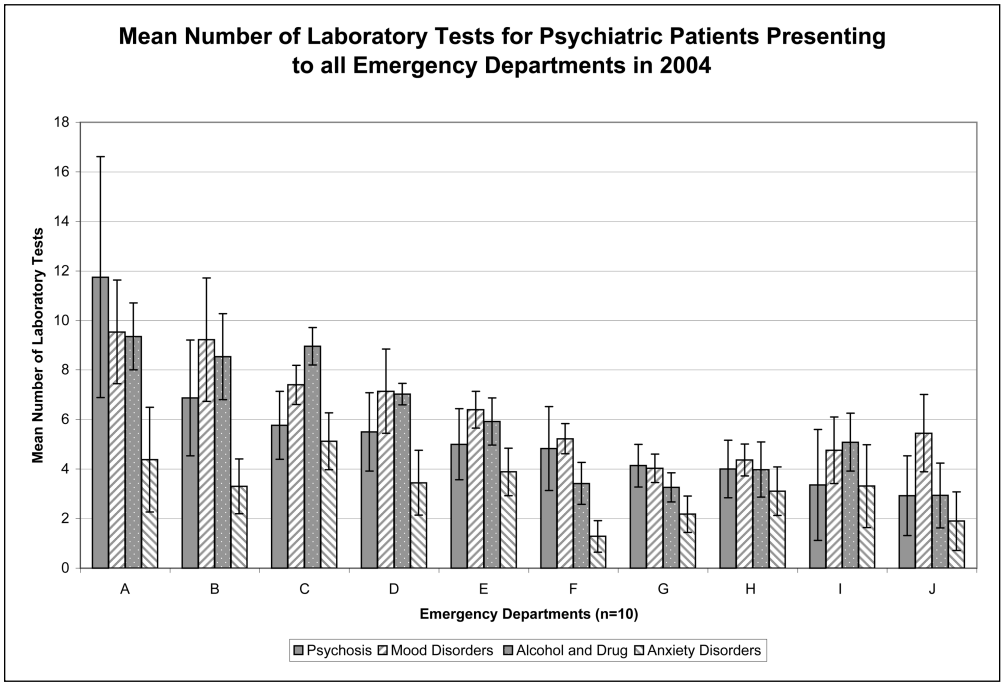
Keith Corl, MD, Michael J. Mello, MD, MPH, Janette Baird, PhD, Liudvikas Jagminas, MD, Michael Siclari, MD, Ali Kazim, MD

Patients who present to the emergency department (ED) with psychiatric symptoms must undergo "medical clearance" prior to assessment and transfer to a psychiatric service. This term refers to the medical evaluation of patients with possible psychiatric illness to identify patients who have acute medical illnesses that cannot be safely treated by an inpatient psychiatric service.

There is no universally accepted protocol for medical clearance of psychiatric patients. A literature review shows that a complete history with a review of systems, vital signs, a physical exam, and a mental status exam are useful for detecting underlying medical problems in patients presenting with psychiatric complaints.[1] Several studies have examined the utility of routine laboratory tests in this population. In a retrospective review of 212 patients presenting to Los Angeles County & University of Southern California Medical Center, of the 80 patients who presented with isolated psychiatric complaints, none had screening laboratory or radiographic findings that changed patient management or disposition.[2] In a randomized trial, researchers found that routine drug screening in a psychiatric emergency service did not alter disposition, management, or length of stay when compared to testing when clinically indicated.[3]

Important to this debate is the acknowledgement that included in the population of psychiatric patients presenting to the ED are several subsets of patients who are at increased risk of having organic pathology present with psychiatric symptoms. These high-risk groups include the elderly, patients with no prior psychiatric history, substance abusers, and patients with preexisting medical problems.[1] In one study of 100 consecutive patients presenting with new onset psychiatric symptoms, 63% had an identifiable organic etiology.[4] A 1992 literature review found that the percentage of clinically significant laboratory results (i.e. results that altered care) from routine screening ranged from 0.8% to 4.0%. Based on these findings, researchers advocated that physicians use their clinical judgment when ordering laboratory tests for psychiatric patients.[5] After a 2004 literature review, researchers concluded that no laboratory investigation is required unless clinically indicated, in patients who have a previous psychiatric history and established psychiatric diagnosis.[1] They further recommended that for patients over 60, patients presenting with new psychiatric symptoms, substance abusers, or patients with concurrent/established medical complaints, a Chem-7, CBC, blood alcohol level, and a urine drug screen should be obtained along with other clinically indicated laboratory tests. In a 2006 clinical policy statement, the **American College of Emergency Physicians (ACEP)** asked: "What testing is necessary to determine medical stability in alert, cooperative patients with normal vital signs, a noncontributory history and physical examination and psychiatric symptoms?" and then reviewed the relevant literature. Based on Class III literature, they recommended that in an adult patient presenting to the ED with primary psychiatric complaints, the history and physical should drive patient diagnosis. They concluded, "Routine laboratory testing of all patients is of very low yield and need not be performed as part of the ED assessment."[6]

Unnecessary laboratory testing consumes time, resources, and money and contributes to ED overcrowding. Identifying inconsistency in the medical clearance of psychiatric patients and the factors driving this inconsistency is needed. This study sought to describe the aggregate laboratory ordering practices of emergency departments across the state when medically clearing a psychiatric patient. Our intent was to not to identify which tests are best, but to describe variation between departments in how they evaluate patients with psychiatric illness.



Materials and Methods

Study Design

This is a retrospective analysis of a single health insurer's database of laboratory testing performed for the medical clearance of psychiatric and substance abuse patients presenting to the Emergency Department. Study subjects were evaluated at the state's ten adult EDs from January 1st to December 31st, 2004. This study examined patients age 18 years or older, presenting to the ED with a psychiatric or substance abuse chief complaint (discharge ICD-9 diagnosis of 291 to 314). Only patients ultimately given a psychiatric diagnosis were included. Patients who were found to have an acute medical problem as well a potential concurrent or related psychiatric illness were excluded. Annual censuses of the EDs for 2004 ranged from 30,000 to 85,000 visits. All patients had the same commercial health insurance.

Demographic patient data and the number of laboratory tests performed per visit were provided by the insurer, which, in 2004, covered 62% of the state's 1,080,632 citizens.[7]

Data Collection, Processing, and Primary Outcome

Data were collected on the primary psychiatric diagnosis, age and gender of the patient, hospital of ED visit, and the number of medical clearance tests performed. Patients were grouped in one of four categories based upon their ICD-9 diagnosis: Psychosis (291.0 – 295.9, 297.1 – 298.9, and 310.2), Mood Disorders (296.0 – 296.99, 311, and 313.0), Anxiety (300.0 – 300.9, 306.0 – 306.1, and 308.0 – 309.9), and Alcohol or Drug Abuse (303.0 – 303.92, and 304.0 - 305.92). The mean number of medical clearance tests per patient was the primary outcome measure of interest. Tests with multiple components such as a CBC or a Basic Metabolic Panel were counted as one. Data were analyzed using SAS for Windows version 9.1 (SAS Institute, Inc. Gery, NC).

Primary Data Analysis

We conducted a three-way **Analysis of Variance (ANOVA)** using a General Linear Modeling approach to assess the main effects of psychiatric diagnosis, gender, and hospital of ED visit on the number medical clearance tests received by the patients. *Post hoc* follow-up tests using Tukey's Standardized Range Test were conducted to examine pairwise differences in the number of tests conducted as a function of hospital of ED visit, gender, and diagnosis.

Results

A total of 2291 patients were included in the analysis. The mean patient age was 34 years (SD = 15.5); 54% were female. Across the sample the mean number of laboratory tests performed per patient evaluation was 5.1 (SD = 4.6). The results of the data analysis demonstrated three main findings.

First, to determine if medical clearance tests significantly varied in our sample across the hospitals of ED visit we controlled for age and ICD-9 diagnosis in the ANOVA analysis. The analysis showed that number of laboratory tests used to medically clear a psychiatric patient significantly varied according to the hospital of patient presentation ($F(9,2289) = 6.13$, $p < .001$). (Figure #1) Follow up Tukey's tests showed that two EDs administered significantly more medical clearance tests across all psychiatric diagnoses compared to state peers.

Next, we analyzed the data to see if the psychiatric diagnosis had an effect on the number of medical tests. Patients presenting with the ICD-9 grouping of anxiety disorder received significantly fewer medical clearance tests in comparison with the other diagnostic groupings ($F(3, 2289) = 6.01$, $p < .001$). There were no significant differences in the number of laboratory tests used to medically clear patients among the ICD-9 groupings of psychosis, mood disorder, or alcohol and drug use.

In summary, after controlling for both age and ICD-9 psychiatric diagnosis there were still significant differences in medical clearance practice as a function of hospital of ED visit.

Limitations

An important caveat to the conclusions that can be drawn from this study is that the data, while covering nearly two thirds of the state's population, did not include patients with Medicare, Medicaid, or the uninsured. These populations are potentially different than the two-thirds of the population with this commercial insurance and our findings may not be generalizable to them. Nevertheless, we intended only to describe variability in how psychiatric patients are evaluated in EDs: having government-provided or no insurance is unlikely to account for the variability in the medical clearance process.

Table 1. Mean Number of Laboratory Tests for Psychiatric Patients Presenting to all Emergnecy Departments

	Alcohol and Drug			*Anxiety Disorders*			*Mood Disorders*			*Psychosis*			*All Psychiatric Diagnosis*		
Hospital	mean	SD	CI	mean	SD	CI	mean	SD	CI	mean	SD	CI	mean	*SD*	*CI*
A	9.4	4.6	[8.0-10.7]	4.4	5.3	[2.3-6.5]	9.5	5.4	[7.5-11.6]	11.8	7	[6.9-16.6]	8.5	5.6	[4.7-9.6]
B	8.5	4.3	[6.8-10.3]	3.3	4	[2.2-4.4]	9.2	5.4	[6.7-11.7]	6.9	5.7	[4.5-9.2]	6	5.2	[2.9-6.9]
C	9	4.6	[8.2-9.7]	5.1	5	[4.0-6.3]	7.4	5.2	[6.6-8.2]	5.8	5.8	[4.4-7.1]	7.3	5.3	[1.8-7.7]
D	7	2.8	[6.6-7.5]	3.5	3	[2.1-4.8]	7.1	3.2	[5.4-8.8]	5.5	3.4	[3.9-7.1]	6.6	3.1	[1.4-7.0]
E	5.9	3.6	[5.0-6.9]	3.9	3.6	[2.9-4.8]	6.4	2.8	[5.7-7.1]	5	4.4	[3.6-6.4]	5.4	3.7	[1.4-5.9]
F	3.4	2.9	[2.6-4.3]	1.3	2	[0.6-1.9]	5.2	2.7	[4.6-5.8]	4.8	3.7	[3.1-6.5]	3.8	3.1	[0.9-4.3]
G	3.3	4.4	[2.7-3.9]	2.2	3.6	[1.4-2.9]	4	4.4	[3.5-4.6]	4.1	4.3	[3.3-5.0]	3.5	4.3	[0.6-3.8]
H	4	3.8	[2.9-5.1]	3.1	4.1	[2.1-4.1]	4.4	2.7	[3.7-5.0]	4	2.8	[2.8-5.2]	3.8	3.5	[0.9-4.3]
I	5.1	4.6	[3.9-6.3]	3.3	4.6	[1.6-5.0]	4.8	3.4	[3.4-6.1]	3.4	4.3	[1.1-5.6]	4.6	4.5	[1.8-5.3]
J	2.9	2.6	[1.6-4.2]	1.9	2.7	[0.7-3.1]	5.5	3.6	[3.9-7.0]	2.9	3	[1.3-4.5]	3.5	3.3	[1.4-4.3]

Another caution is that this retrospective analysis used final diagnosis as the qualifier to be entered into the database. If a patient presented with a psychiatric complaint but was found to have no psychiatric illness but rather a medical illness, they would have not been included in this study's database. Thus, no inference can be made on what test should or should not be utilized or the optimal number of tests needed for medical clearance. We only document the inconsistencies in laboratory ordering practices across our state when evaluating patients who are ultimately diagnosed with a psychiatric illness.

Discussion

Our data illustrate the lack of consistency in the number of laboratory tests utilized during the medical clearance of psychiatric patients presenting to the ED. A patient presenting with a diagnosis of psychosis at one ED may receive up to four times the number of laboratory tests the same patient would receive if they presented to another ED. While the precise etiology of this may be unknown, and is likely to be multifactorial, several can be hypothesized. Knowledge of the literature and individual comfort level for ruling out a medical etiology without additional laboratory tests varies from physician to physician. Certain key physicians may either by example or departmental policy dictate departmental practice on this issue. Nursing may have variable authority in ordering laboratory studies between EDs; this may contribute to variability between departments. Long-standing working relationships of admitting patients from a particular ED to a psychiatric inpatient service may affect the mean number of laboratory tests ordered. The ability of an inpatient psychiatric service to obtain laboratory tests after admission is likely to decrease the number of labs are obtained in the ED. Emergency departments themselves may have adopted practice patterns that affect ordering practices (i.e. laboratory tests that are sent before the patient is seen by a physician).

Our data demonstrate inconsistent testing across emergency departments when medically clearing equivalent patient populations. Laboratory testing consumes the time and resources of EDs, which in turn exacerbates the nationwide problem of ED overcrowding. Identification of this problem is a first step. A solution depends upon a collaborated effort between the emergency medicine and psychiatric communities. The goal should be a set of evidence-guidelines that would standardize the process of medical clearance and outline the proper use of laboratory tests when admitting a psychiatric patient from an ED to an inpatient ward. Such a set of guidelines would need to address the varying needs of specific psychiatric subset populations, specifically the elderly, patients with no prior psychiatric history, patients with preexisting medical problems, and substance abusers. While the ACEP's 2006 Clinical Policy statement is a tremendous national accomplishment for the specialty, further work is needed to adopt current recommendations into clinical practice at the state and local levels. The Massachusetts ACEP "Joint Task Force Consensus Guidelines on the medical clearance exam and the use of toxic screens for the evaluation and management of the psychiatric patient in the Emergency Department "[8] may serve as a model for drafting similar guidelines in other states. Ultimately, a protocol that would be prospectively tested would be ideal to direct further clinical policy.

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Keith Corl, MD, is a 3rd year Resident, Emergency Medicine Program, Warren Alpert Medical School of Brown University.

Michael J. Mello, MD, MPH, is Assistant Professor of Emergency Medicine and Community Health, Warren Alpert Medical School of Brown University.

Liudvikas Jagminas, MD, is Physician-in-Chief of Emergency Medicine, Memorial Hospital of RI, and Associate Professor of Emergency Medicine, Warren Alpert Medical School of Brown University.

Janette Baird, PhD, is Assistant Professor (Research), Warren Alpert Medical School of Brown University.

Michael Siclari, MD, is a staff physician at Providence VA Medical Center Emergency Department and Memorial Hospital Rhode Island Emergency Department.

Ali Kazim, MD, is Clinical Associate Professor of Psychiatry and Director of Emergency and Correctional Psychiatry, Warren Alpert Medical School of Brown University.

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Correspondence:

Keith Corl, MD
Department of Emergency Medicine
593 Eddy Street
Providence RI 02903
(315)-430-4876 cell
phone: (401)-444-5826
keith_corl@brown.edu

Abstracts: Rhode Island Chapter, American College of Physicians 2008 Annual Meeting Associates Forum Competition Winners

The Rhode Island Chapter of the American College of Physicians in April of 2008 hosted its Annual Associates Forum Competition and Podium Presentation. There were over seventy submissions from Residents in the four teaching programs at Rhode Island hospitals. A committee of program directors made the difficult choice of picking seven winners.

At the Annual meeting we had a distinguished panel of three judges as well as over 100 attendees listen to the presentations. There were a mixture of Clinical Vignettes with a literature review and Original Research. All the presenters had outstanding projects, with topics ranging from a "Fever of Unknown Origin" to the "Quality of Sleep in Hospitalized Patients".

The seven podium presenters each received a plaque and a cash reward from the College Chapter. It is reassuring and inspirational to know that these outstanding Associates are the future of medicine in the United States. Congratulations to all the participants in this year's competition.

– N.S. Damle, MD, FACP
Governor
Rhode Island Chapter of the
American College of Physicians

Fever of Unknown Origin

Nicole Theodoropoulos, MD, Associate, and Bethany Gentilesco, MD
Warren Alpert Medical School of Brown University Department of Internal Medicine, The Miriam Hospital

DC, a 41 year-old man with a history significant for adult onset diabetes mellitus and recent immigration from Brazil, presented to the hospital with daily fevers for 5 weeks. He also complained of vague diffuse abdominal pain associated with nausea, history of watery diarrhea (now resolved) weight loss. The patient had traveled from Brazil through the Americas to Rhode Island, living outdoors and drinking brackish water. Several members of his traveling party fell ill with similar symptoms. He did not recall any rashes or insect bites during his travels.

Physical exam on admission revealed temperature of 103.2 degrees Fahrenheit and vital signs otherwise within normal limits. Abdominal exam revealed diffuse tenderness, slightly worse in the right upper quadrant and mild splenomegaly. No lymphadenopathy or skin changes were noted and physical exam was otherwise unrevealing.

Labs upon admission were notable for pancytopenia (WBC 1600 with 71% segmented cells and 4% bands, hemoglobin 9.7 g/dL and platelets 67,000). Mild hemolysis was noted with 1+ schistocytes on peripheral blood smear, reticulocyte count 5%, LDH 552 IU/L, Haptoglobin 17 mg/dL. Liver function tests showed elevated AST 127 IU/L, ALT 242 IU/L, Alkaline Phosphatase 263 IU/L and hypoalbumenia 2.5 g/dL. Ferritin was elevated at 11,711 ng/mL. A CAT scan of the abdomen revealed only mild splenomegaly. Blood and urine cultures were negative. An extensive work up for fever of unknown origin followed. Ehrlichia, and Babesia titres, HIV ELISA and viral load, parasite smears x 3, and hepatitis serologies were all negative. EBV and CMV titres were IgG positive only. PPD was placed and did not react. Empiric treatment with Ceftriaxone for possible typhoid fever was started without good clinical result. A continuing FUO work up was pursued. FTA-ABS was positive but RPR was negative. Stool studies were all negative. Brucella, tularemia, histoplasma, coccidoides, Q fever, blastomycoses, leptospira, strongyloides and bartonella serologies were all negative. Typhoid, dengue, parvovirus, schistosomiasis serologies all showed evidence of prior exposure but not acute infection. During his hospital stay, a new genital ulcerating lesion was noted. HSV DFA was positive upon swab of this lesion and the patient was placed on Valcyclovir for treatment.

The patient underwent bone marrow biopsy, which revealed poorly formed granulomas but negative cultures and AFB. Liver biopsy was done, which also showed microgranulomas. On hospital day 26, despite no organisms being identified on liver or bone marrow biopsy, Leishmaniasis titres were sent. His Leishmaniasis titres returned as IgG + for L Donovani and L. Braziliensis. The CDC was contacted and his original liver biopsy sample was sent to the Armed Forces Institute of Pathology. Further review there by an expert in the disease identified the intracellular amastigotes consistent with leishmaniasis. On hospital day 42, he was started on liposomal amphotericin for treatment of leishmaniasis. After 3 days of therapy, he defervesced. His labs did not improve, but he was discharged home in stable condition on hospital day 48 with outpatient infusion of day 14 and day 21 liposomal amphotericin.

Discussion: There are an estimated 500,000 new cases of symptomatic **visceral leishmaniasis (VL)** a.k.a kala-azar yearly; 90% of cases are reported from endemic regions of Bangladesh, India, Sudan and Brazil. Visceral disease is most often caused by the species of the *L. donovani* complex, for which our patient had IgG positivity. Leishmaniasis parasites are carried by the sandfly vector. Clinical disease occurs on a spectrum with marked immune response causing mucocutaneous leishmaniasis at one end and lack of granulomatous inflammation (ie visceral leishmaniasis and diffuse cutaneous leishmanisis) at the other end. Five classic features make up VL disease: organomegaly, fever, cachexia, pancytopenia and hypergammaglobulinemia. Darkening of the skin also occurs commonly in India with VL. These features in a patient living in an endemic area should highly suggest the diagnosis. Diagnosis is confirmed by visualizing amastigotes in tissue or promastigotes in culture. Splenic aspiration is the most sensitive, followed by bone marrow aspiration. Lymph node and liver biopsy can also be used. Antileishmanial antibodies are often positive in high titers in im-

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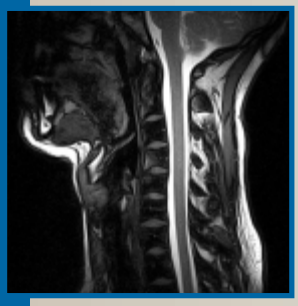

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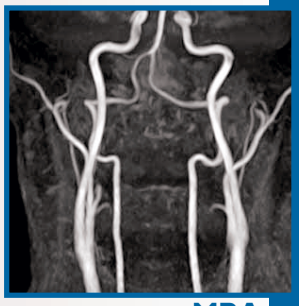

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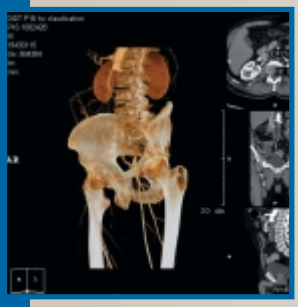

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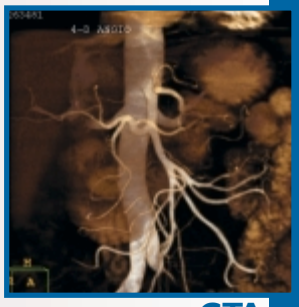

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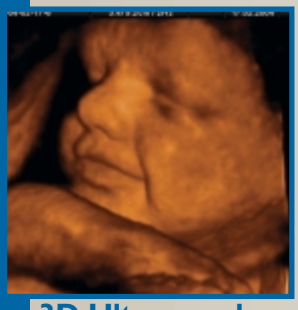
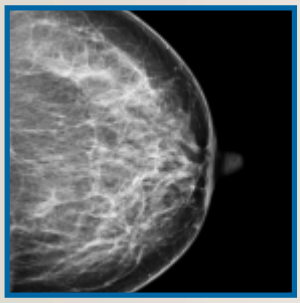
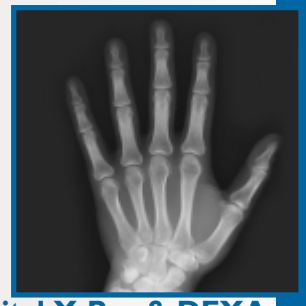


3D Ultrasound



Digital Mammography



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munocompetent patients with VL. In summary, visceral leishmaniasis should be on the differential for fever of unknown origin in patients traveling to or from endemic areas.

E-mail: ntheodoropoulos@lifespan.org
Program Director: Dominick Tammaro, MD, FACP

Hypokalemic Thyrotoxic Periodic Paralysis in a Young African American Male

Ravi Gupta, MD, Associate; Gerardo Carino, MD
Warren Alpert Medical School of Brown University Department of Internal Medicine, The Miriam Hospital

A 26-year-old African American gentleman presented with a one-day history of profound upper and lower extremity weakness and a one-week history of watery diarrhea. For two days prior to admission, when the patient awoke he noted extreme difficulty moving. The symptoms would gradually resolve and he would be able to carry out his daily activities. However, on the day of admission he awoke with weakness so profound that he could not stand up. He then became anxious and noted SOB, nausea, and diaphoresis, at which point he called rescue and was brought to the hospital. ROS were notable for several months of DOE, frequent palpitations, and insomnia. The patient denied using any medications or illicit substances. Initial examination was remarkable for tachycardia, thyromegaly, and 3+ reflexes. Laboratory results demonstrated hypokalemia (1.3) and hypophosphatemia (<1.0). Thyroid function studies revealed hyperthyroidism (TSH: <0.03, FT4 : 4.09, T3: 447).

The patient's EKG showed atrial fibrillation with LAD. He was admitted to the ICU, where his potassium was repleted and he was started on PTU and propanolol. It was felt that his hyperthyroidism was secondary to Graves Disease. He clinically improved initially; however, his course was complicated by SOB on HD #2. A CT Angiogram demonstrated mediastinal LAD and bilateral infiltrates, which were thought to be secondary to his thyroid disease and atrial fibrillation, respectively. After complete electrolyte repletion he no longer noted any weakness. He returned to sinus rhythm and his SOB resolved. He was discharged on PTU and propranolol and was scheduled for endocrinology follow-up.

Discussion: **Thyrotoxic Periodic Paralysis** (**TPP**) is a rare neuromuscular disorder characterized by concomitant thyrotoxicosis, paralysis, and hypokalemia. It typically affects Asian men between the ages of 30-50, although it can occur in other ethnic groups. The pathophysiology of TPP is believed to be from increased Na+ - K+ - ATPase muscle ion channel activity in the setting of thyrotoxicosis. This results in increased cellular uptake of potassium, which can further be exacerbated by a high insulin state, causing paralysis in genetically predisposed persons. TPP clinically presents as weakness or flaccid paralysis occurring either a few hours following vigorous exercise, or early in the morning after a high-carbohydrate meal. The degree of muscular involvement and the severity of the attacks can vary widely, although characteristically there is greater proximal muscle involvement. The diagnosis is based on the absence of family history, and the presence of biochemical thyrotoxicosis and hypokalemia. Treatment consists of potassium supplementation, b-blockade, and anti-thyroid medications.

Although TPP usually has a benign course, early diagnosis and restoration of the euthyroid state is essential to prevent recurrent, potentially life-threatening, episodes of paralysis.

Email: rgupta818@gmail.com
Program Director: Fred Schiffman, MD, FACP

Predicting HIV Viral Load by Immunological Trends: Implications for Identification of Treatment Failure in Resource-poor Settings

Philip A. Chan, MD, Fizza S. Gillani, MD, Susan Cu-Uvin, MD, Charles C. Carpenter, MD, Rami Kantor, MD
Departments of Medicine and Division of Infectious Diseases, Warren Alpert Medical School of Brown University

Treatment failure during **highly activated anti-retroviral therapy** (**HAART**) is best defined as a persistent detectable HIV **plasma viral load** (**PVL**). In resource-poor settings, laboratory assays for PVL are often unavailable due to financial and infrastructure constraints. The paucity of available second-line antiretroviral drugs makes deciding when to change HAART a challenge. Recognizing these limitations, the World Health Organization published HIV treatment guidelines in 2006 and defined treatment failure based on immunological criteria as: 1) A decrease of CD4 cell count to pre-therapy baseline levels or below; 2) A 50% decrease from the on-treatment peak value; and/or 3) Persistent CD4 count levels below 100 cells/mm3. Clinical practice in many resource-poor settings rely on at least a greater than 25% decrease in CD4 cell count to define treatment failure during HAART. Current literature suggests that CD4 counts are not strongly associated with PVL and that CD4 percent may be a more accurate predictor of PVL. To further define the relationship between CD4 cell count, CD4 percent, and PVL, we obtained data on 303 patients from the outpatient HIV clinic at The Miriam Hospital. Patients were eligible if they were on HAART for at least six-months, and had CD4 and PVL data available during this time. We examined proportions of virologic failure based on immunological trends using the Chi Square and Fisher Exact tests. A > 10% decline in CD4 percent over a six month time period was significantly more likely to predict a detectable PVL when compared to any decrease in absolute CD4 cell count (18/41 patients with a CD4 percent decrease > 10% had an undetectable PVL, versus 71/102 for any decrease in CD4; p=0.007). On the other hand, a > 25% decline in absolute CD4 cell count was not able to predict a detectable PVL better than using any decrease in CD4 percent (p>0.10). A > 50% decrease in absolute CD4 cell count was only significantly better at predicting a detectable PVL for a decreasing CD4 cell percent less than 5% (p=0.04). A persistent CD4 level below 100 cells/mm3 compared to a persistent CD4 percent below 7% was not able to better predict a detectable PVL (p=0.62). We conclude that decreases in CD4 percent may be a more accurate pre-

dictor of a detectable PVL and thus of treatment failure. The incorporation of CD4 percent trends as a secondary marker to guide treatment decisions may be helpful in resource poor settings.

Email: pchan@lifespan.org
Program Director: Michele Cyr, MD, and Dominick Tammaro, MD

Methicillin-Resistant Staphylococcus Aureus Colonization of Surgical and Medical Residents

Anna A. Barbosa, MD, Associate, Department of Internal Medicine; Leonard A. Mermel, DO, FACP, Department of Epidemiology and Infection Control, Rhode Island Hospital, Warren Alpert Medical School of Brown University

In healthcare settings, transmission of **Methicillin-Resistant Staphylococcus aureus (MRSA)** to patients is most often from **healthcare workers (HCWs)** who have less than optimum hand hygiene. According to CDC guidelines, surveillance cultures for MRSA are not routinely recommended for HCWs unless epidemiologically linked to clusters of cases among patients. Rates of MRSA colonization of HCWs are generally unknown, particularly among house staff. Similarly, it is unknown if differences exist in MRSA colonization among medical and surgical house officers as a result of differences in exposure, procedures done, etc. The purpose of our study was to determine the prevalence of MRSA carriage in medical and surgical house staff. Our null hypothesis was that there was no difference between the two groups of house officers.

METHODS: During a one-month period, fifty medical and fifty surgical residents at Rhode Island Hospital were enrolled in a prospective, point-prevalence survey of MRSA nasal carriage. In addition to obtaining nares cultures for MRSA, each resident completed a brief questionnaire about their perceptions of hand hygiene and isolation precautions used when examining patients with MRSA. This investigation was approved by the hospital IRB. A 2-tailed Fischer exact test was used for statistical analysis.

RESULTS: Five surgery residents (10%) and zero medical residents were found to have a positive nares culture for MRSA (p=0.03). Of the surgery residents who were MRSA-positive, 3 of 22, 2 of 9, and 0 of 19 were PGY1, PGY2, and PGY3-10, respectively (p=0.1 for MRSA carriage among PGY1 and 2 vs. PGY3-10). CONCLUSION: There is a higher prevalence of MRSA in the nares of surgical vs. medical house staff. The reason for this difference is not known, but may be related to greater direct contact with MRSA-infected wounds among surgical residents vs. medical residents. There may be a higher risk of MRSA carriage among surgical residents earlier in their training when they have a more direct role in post-operative wound care. Further research is necessary to help fill gaps in our knowledge of colonization in house staff.

Email: annaffabarbosa@hotmail.com
Program Director: Dominick Tammaro, MD

Genetic and Functional Adaptation of Pancreatic Beta Islets To Pregnancy: Potential for Gene Therapy In Diabetic Patients

Georg Elias MD, Melissa Brown, PhD, Luca Cicalese, MD, Cristiana Rastellini, MD, Boston University, Roger Williams Medical Center, and.The University of Texas Medical Branch, Galveston, TX

In vitro studies have demonstrated that pregnancy-influenced murine pancreatic beta cells are capable of secreting more insulin during pregnancy than non pregnant controls. Also it has been observed that murine pancreatic beta cells undergo active proliferation during the last week of pregnancy and return to a quiescent status two days post delivery (pd2).

To the best of our knowledge there have been no studies to evaluate the function of pancreatic islets from pregnant mice after transplantation into non pregnant mice.

AIMS: To prove that islets, under the influence of a gestational environment, exhibit improved functionality, even when ectopically transplanted into non pregnant mice, and to determine the genetic profile in pancreatic islet during pregnancy.

METHODS: Diabetes was chemically induced in female mice recipients and was defined by blood sugar (BS) 300 mg/dl. Islets were isolated from syngeneic pregnant day 7, day 15, pd2, and non pregnant female donors. Recipient mouse received islet transplantation under one kidney capsule. Recipient mice were divided into three groups. The first group received full mass transplantation of 600 islet equivalent (IEq), the second received suboptimal mass of 400 IEq, and the third group received marginal mass of 200 IEq. Blood sugar was checked three times a week. Reversal of diabetes was defined as BS less than 200 mg/dl. Grafts were later harvested and analyzed. Gene profile was performed after islets were isolated from pregnant mice on days 7, 14, 15, 18, pd2 and control non pregnant mice.

RESULTS: Reversal of diabetes was observed in 75% of marginal mass recipients from pregnancy day 15 donors, and 100 % in marginal mass recipients from pd2, but there was no reversal in recipient from day 7 and control none pregnant donors. The statistically significant and two fold differentials in genetic venations were as follow: Control versus day 7 and day 14: no difference. Control versus day 15: 34 genes Control versus day 18: 54 genes Control versus pd2: 23 genes Some of these genes are related to proliferation, migration, secretion, or apoptosis.

CONCLUSION: Pancreatic islets isolated from animals on their last third of pregnancy (P15 and pd2) demonstrate improved functionality and reverse diabetes, preserving long-term euglycemia, in a marginal mass transplant model. We have identified a number of genes the expression of which is significantly changed during pregnancy in association with islet proliferation that could be a potential for gene therapy in diabetic patients.

Email: georgeeliasmd@gmail.com
Program Director: Alan B. Weitberg, MD

Effects of Erythropoietin Adjust Automated Protocols on Hemoglobin Levels in ESRD Patients

Luiz M. Kolankiewicz, MD, Jerome S. Tannenbaum, MD, PhD, FACP, Marcos Rothstein MD, FACP, Marc S. Weinberg MD, FACP, Roger Williams Medical Center, Boston University School of Medicine, DSI Renal, Inc. Nashville, TN, and Washington University Medical School, St. Louis, Missouri

Background: Recent anemia studies have demonstrated increased mortality in patients with hemoglobin (Hb)levels>13g%. As a result, the FDA instituted a Black Box Warning "to use the lowest dose of erythropoietin stimulating agents (ESAs) that will gradually increase the hemoglobin concentration to the lowest level sufficient to avoid the need for red blood cell transfusion." In addition, other recent clinical trials have shown adverse outcomes with Hb<11g%. We evaluated Hb variability following alterations in erythropoietin adjust protocols with goals to reduce subjects with Hb>13g%. Changes in Hb<11g% and >13g%, and related variables, were analyzed to determine effects of ESA dose on hemoglobin. Methods: We designed a retrospective cohort study in 7021 patients treated in 120 dialysis facilities at DSI Renal, Inc. from January-December,2007. We investigated variability in serum Hb levels, for Hb<11g% and Hb>13%, and other variables (Ferritin-Reticulocytes-URR-Iron Saturation). Comparisons were made among three groups; the original erythropoietin anemia protocol-A (Jan-April (pre-FDA)), protocol-B (May-Aug (post-FDA)) and protocol-C (Sep-Dec (modified to optimize Hb target 11–12g%)). The intent of protocol-B was to reduce the % of dialysis patients with Hb>13g%. After demonstrating a main effect by ANOVA, Students t-test was performed utilizing Bonferroni correction factor.

Results: In subjects with Hb<11g%, ANOVA showed p=0.0045 for protocol periods A, B and C. Students t-test between protocols A-B(p=0.0005), and B-C(p=0.0226) were significant. For Hb>13g%, ANOVA was p=0.0061 with changes only from A-B(p=0.004), although there was an arithmetic increase from B-C(p=0.054). Other parameters analyzed showed no significance by ANOVA (Ferritin-Reticulocytes-URR). Although Iron Saturation was significant (p=0.033) by ANOVA, Students t-tests between A-B and B-C were non-significant. Nearly twice as many patients had a significant increase in Hb<11g% compared to a reduction in Hb>13g% during protocol B.

CONCLUSIONS: These data demonstrated a significant increase in subjects with Hb<11g% between A-B and a reduction from B-C, while for Hb>13g%, there was a significant reduction between A-B, and an arithmetic, but non-significant increase during B-C.These changes may be related to delayed erythropoietin effects that may occur over several weeks in response to changes in total ESA dose, or other influences on Hb levels. Further analysis is required to better understand relationships between hemoglobin variability, total erythropoietin dose, the number of months out of the established Hb target and their effect on mortality.

Email: kolanki@yahoo.com
Program Director: Alan B. Weitberg, MD, FACP

Quality of Sleep In Hospitalized Patients

Paras Patel, MD, Rakesh Gupta, MD, Roger Williams Medical Centerl/Boston University School of Medicine

Background: Sleep affects health, daytime function and quality of life. Hence measurement of sleep quality in hospitalized patients is important as it may offer an intervention target to improve clinical outcomes. A basic assessment of sleep quality can be done with sleep diary, sleep log and sleep questionnaire. Insomnia is a subjective complaint of dissatisfaction with the quantity, quality or timing of sleep. Insomnia affects approximately 12 to 25% of the general population and is more prevalent in hospitalized patients. In hospitalized patients, the most common causes of acute insomnia includes the effects of illness, environmental sleep disruption, medication, anxiety and depression. We conducted a questionnaire study to understand quality of sleep and factors affecting sleep in hospitalized patients.

Methods: This single-centre prospective study involved an assessment of sleep quality for consenting patients admitted to the general medical floor at RWMC. Each patient was given questionnaires asking them about their quality of sleep, use of sleep aids, factors disrupting sleep as related to the illness or hospital environment. They completed a sleep diary and a daily questionnaire during hospital stay. A final discharge day questionnaire was completed summarizing their sleep during hospital admission. Each patient was asked to make any additional comments about their sleep.

Results: 35 patients were enrolled at random (19 males, 16 females) who suffered from multiple chronic diseases. The TST at home was 8.8 + 1.6 hours versus 9.4 + 1.1 hours in hospital (p=0.04). Nocturnal awakenings were increased during hospital stay (1.66 + 0.64) compared to home (1.02 + 1.25, P=.009). Daytime naps at home were reported by 1% compared to 99% in hospital. The average total daytime nap time was 1 hour at home and 3 hours in hospital. 43% of subjects received some kind of sleeping aid at home compared to 74% in hospital.Patients reported a very high impact of hospital environment on their sleep – 9 on a 0-10 scale. Their illness was also perceived to be impacting quality of sleep - score of 7 on the same scale of 1-10.

Conclusion: Overall patients had more fragmented sleep even though the total sleep time was increased in the hospital. Patients reported a bigger impact of hospital environment (noise, TV, nursing, roommates, blood draws, vital checks etc) than medical illness on sleep quality. More nighttime awakenings led to increase in daytime naps to compensate for the total sleep time. Data regarding differences due to hypnotic administration during hospital stay will also be presented (not yet analyzed).

Email: paras_patelmd@yahoo.com
Program Director: Alan Weitberg, MD, FACP

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GERIATRICS FOR THE PRACTICING PHYSICIAN

QUALITY PARTNERS OF RHODE ISLAND

Quality Partners of RI
Edited by Ana Tuya Fulton, MD

Prognostication: Medicine's Lost Art

Christopher A. Jones, MD

With the recent diagnosis of glioblastoma in Senator Edward Kennedy, the press asked the "time" question: "How much time does he have left?" As we know, most patients succumb within 12-18 months after diagnosis.[1] Estimating disease outcomes within a range can be done with some confidence. It is more difficult to predict the outcome for an individual patient.

Medical prognostication, "a prediction of future medical outcomes of a treatment or a disease course based on medical knowledge," [2] has become something of a lost art. Prognosis, diagnosis, and therapeutics make up the main clinical skills in medical practice. Seventy-five years ago, when most effective medical therapies did not exist, the most skilled physicians were astute diagnosticians and frequent prognosticators.[3] Today, in the exam or intensive care room, discussion focuses on diagnostic and therapeutic options. Prognostication takes a back seat. Some of this relative neglect may come from the hope that prognosis will not be necessary, that cure will be the outcome.

Medicine has delineated four major trajectories for the common causes of death.

The first, sudden death, or a squared death curve, often occurs as a result of trauma, accident, or suicide. Each member of the group is alive and functionally able until death, without antecedent decline in function.

Second, with cancer, a typical death curve can be drawn for each type of malignancy. While the time axis will be shorter and the functional decline steeper for patients with glioblastoma than for those with prostate cancer, a relatively predictable rate of decline to death can be described for incurable malignancy.

The third type is the most difficult to predict - mortality from chronic diseases, such as congestive heart failure (CHF) or chronic obstructive pulmonary disease. The classic death curve shows a years-long, slow decline with intermittent acute crises. After the crises the individual usually recovers, but not to the previous functional level until a final crisis cannot be, or is not, treated; and death occurs.

The final death curve describes the slow languishing of Alzheimer's and other neurodegenerative diseases. This trajectory is shallow, as the functional decline is slow and progressive; it allows for years of very poor function and life quality before death, which often comes following a seemingly minor illness or without a clear precipitant.[4]

After considering which death curve a patient is on, formulating an accurate prognosis requires acknowledging our own fear and bias as physicians. Studies have surveyed physician attitudes about prognostication. Many physicians described prognosticating as stressful and difficult. They believed that patients expected too much certainty, and more than half of physicians surveyed felt inadequately trained in prognosis.[5]

Christakis, et al surveyed 343 physicians regarding their estimation of life expectancy when 468 terminally ill patients were referred to hospice. The patients were 45% male; 65% had cancer. The patients' predicted life expectancy was compared to actual survival. Only 20% of doctors' predictions were accurate, defined as +/- 33% of actual survival. Sixty-three percent were overly optimistic and just 17% were overly pessimistic. Physicians overestimated in either direction by a factor of 5.3.[6]

In another study, treating oncologists predicted survival on average to within 3 months for a cohort of patients with metastatic breast or prostate cancer who lived an average of 9 months.[7] The most experienced physicians were most successful at prognostication. Non-oncologic medical subspecialists were the least accurate prognosticators in this trial, and more likely to be overly pessimistic than other groups. What is more surprising is that longer doctor-patient relationships actually decreased a physician's ability to accurately predict survival. The authors proposed that a "prognosis consult" might be valuable, since non-invested physicians with extensive clinical experience were the most accurate prognosticators.[6]

In addition to knowing the likely death curve for a disease state, it is important to consider functional losses suffered by the patient. Several clinical prediction models exist. The **Karnofsky Performance Scale (KPS)**, first described in 1949 by the American oncologist David Karnofsky, stratifies patients with terminal illness on a scale of 100 (fully functional) to 0 (dead), taking into account self-care, activity, and burden of illness.[8] One early study of the KPS estimated that each increase in 10 points offered another 2 weeks of life expectancy, though this study was designed more for research than clinical application.[9]

The more recent **Palliative Performance Scale (PPS)** takes into account additional functional domains. The PPS scores patients on ambulation, activity and evidence of disease, self-care, oral intake, and level of consciousness.[10] One study involving 773 patients already admitted to a Palliative Medicine unit in Canada noted that PPS score, gender, and age, but not diagnosis were strongly correlated with survival. Of note, the older men had shorter survival.[11]

These scales are useful for thinking about life expectancy for patients in the community and the clinic. As discussed earlier, patients who are hospitalized, particularly those with an acute exacerbation of a chronic disease, are at higher risk for death.

Schema exist for predicting in-hospital mortality from CHF, including a recently published point-system based on the few factors most strongly predicting mortality (age, heart rate, systolic blood pressure, serum creatinine, primary cause of admission, and the presence of left ventricular systolic dysfunction). Derived from data collected from the 48,000-pa-

Tools and Resources:

Palliative Performance Scale:
Available on-line at http://palliative.info/resource_material/PPSv2.pdf

OPTIMIZE-HF heart failure quality improvement study nomogram:
Available on-line at https://www.optimize-hf.org/art/OPT-Mortality.pdf

Home & Hospice Care of Rhode Island
Online resources for performance scales and hospice criteria for chronic disease.
Available on-line at http://www.hhcri.net/guidelines.html

Prognostication, in-depth, detailed review of the literature:
Glare and Sinclair[15]

tient OPTIMIZE-HF heart failure quality improvement study, the scale and nomogram can be found online [https://www.optimize-hf.org/art/OPT-Mortality.pdf].[12]

Patients with advanced stage malignancies are more often concerned with prognosis than are patients with chronic diseases. Experienced oncologists are usually the most able prognosticators for their patients. Generally, patients with metastatic or extensive solid or hematologic cancers who have stopped palliative chemotherapy have fewer than 6 months to live. However, patients with prostate and breast cancers can have a more indolent course. Several sequelae of cancer predict a more limited prognosis. These include malignant hypercalcemia (except in those with newly diagnosed breast cancer or myeloma), malignant pericardial effusion, and neoplastic meningitis. These conditions limit life expectancy to 8-12 weeks. In the case of multiple brain metastases, life expectancy is 1-2 months without radiation and 3-6 months with radiation. [13]

Having an accurate estimation of prognosis has been shown to affect patients' choices regarding treatment, especially regarding emergency and end-of-life care. Murphy et al. asked 287 adults 60-99 years old, without telling them of the true probability of its success, whether they would want CPR in case of cardiac arrest during an acute illness. Forty-one percent initially wanted CPR attempted. After learning that survival to discharge from the hospital ranges from 10-17%, only 22% still wished for resuscitation, and only 6% over the age of 86 wished a resuscitation attempt. When queried about having CPR attempted in the setting of a chronic disease with a one-year life expectancy, only 11% asked for CPR. Upon learning that discharge rates range from 0-5% under this scenario, only 5% preferred that CPR be attempted.[14]

Prognostication is fraught with difficulty, and in an age of advanced and extensive treatment options has become a dinosaur of sorts. Ultimately what is gleaned from research is that knowledge of the death curve of the patient's life-limiting diagnosis can help inform prognosis. Additionally, remembering important co-morbidities and the patient's functional status will facilitate further personalization of prognosis. As physicians, we should know that we tend toward overestimation of life expectancy. Clinical models exist for many common chronic and oncologic diseases that enable physicians to use objective criteria to predict mortality. As difficult a conversation as this can be, patients appreciate knowing their prognosis, even if limited, so they can plan for their remaining time.

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Christopher A. Jones, MD, is PGY-3, General Internal Medicine, at The Warren A. Alpert Medical School of Brown University.

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Health By Numbers
RHODE ISLAND DEPARTMENT OF HEALTH • DAVID GIFFORD, MD, MPH, DIRECTOR OF HEALTH
EDITED BY SAMARA VINER-BROWN, MS

Health Risks Among Rhode Island High School Students, 1997–2007

Donald K. Perry, MPA, and Yongwen Jiang, PhD

The **Centers for Disease Control and Prevention (CDC)** report that 72% of all deaths in the 10-24 age group in the United States result from motor-vehicle crashes, other unintentional injuries, homicides, and suicides. Each year there are 757,000 pregnancies among 15-19 year olds, and an estimated 9.1 million cases of sexually transmitted diseases among persons aged 15–24 years. Almost 59% of deaths among adults over 25 result from cardiovascular disease and cancer. The US Department of Health and Human Services outlined youth-related objectives in their *Healthy People 2010* report.[1]

Several behaviors that typically begin during youth are responsible for these major sources of mortality, morbidity, and social problems; e.g., carrying weapons, physical fighting, attempted suicide, drinking while driving, lack of seatbelt use, lack of bicycle helmet use, unprotected sexual intercourse, tobacco use, unhealthy dietary behaviors, and physical inactivity.[2] This report examines 10-year trends in health risk behaviors among Rhode Island public high school students.[3]

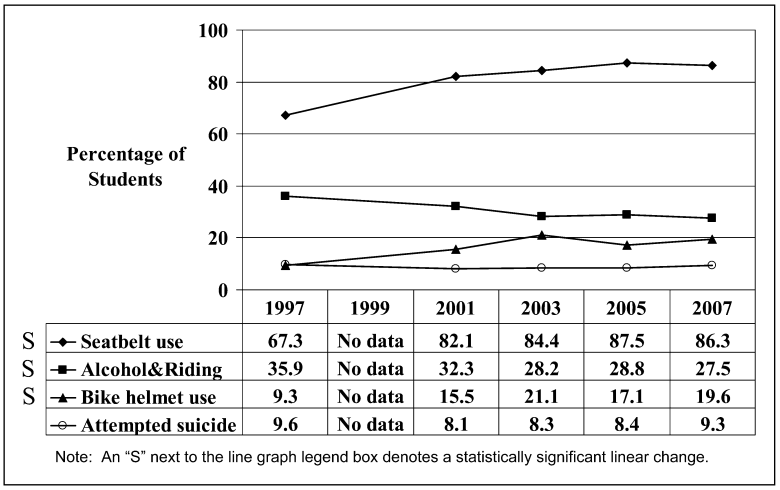
METHODS

The CDC has sponsored a national and state **Youth Risk Behavior Survey (YRBS)** since 1991, including the 2007 YRBS in 60 states and municipalities. Rhode Island has conducted a high school YRBS in odd numbered years since 1995 as a joint effort of the Departments of Health and Education and other state agencies. The voluntary survey is self-administered among randomly selected public high schools and students in grades 9-12.

The YRBS monitors health-risk behaviors related to injuries, tobacco, alcohol and other drugs, sexual behavior, weight and nutrition, and physical activity. This article highlights the prevalence of these behaviors during five survey cycles from 1997-2007. With the exception of 1999 when there were insufficient data, Rhode Island achieved overall response rates greater than 60% in samples of 1,400 to 2,400 high school students in each survey year. These rates were sufficiently high to enable the CDC to weight the self-reported data, which are then considered representative of the entire public high school population.

RESULTS

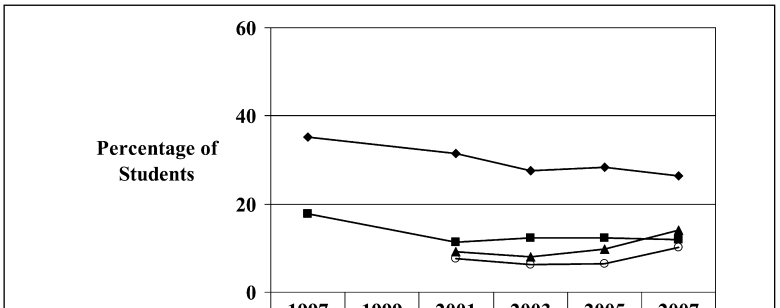
There were statistically significant trends for 13 of 16 key behaviors presented here of which all but 3 represented improvements in healthy practices. These behaviors are a cross-section of the over 80 questions in the YRBS. Regarding injuries (Figure 1), there were improving trends between 1997 and 2007 in the proportion of students using seatbelts (67% to 86%), wearing bicycle helmets (9% to 20%), and riding with a driver who has been drinking (36% to 28%). In contrast, attempted suicide (in past year) remained unchanged at nearly 10%.



		1997	1999	2001	2003	2005	2007
S	Seatbelt use	67.3	No data	82.1	84.4	87.5	86.3
S	Alcohol&Riding	35.9	No data	32.3	28.2	28.8	27.5
S	Bike helmet use	9.3	No data	15.5	21.1	17.1	19.6
	Attempted suicide	9.6	No data	8.1	8.3	8.4	9.3

Note: An "S" next to the line graph legend box denotes a statistically significant linear change.

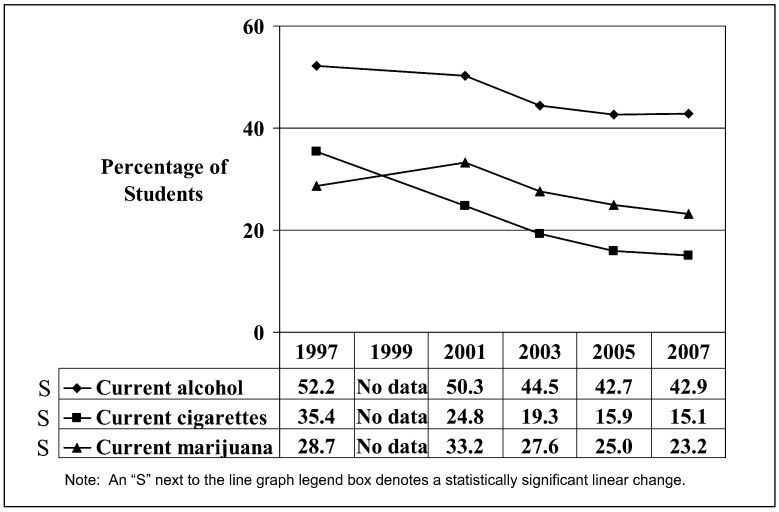
Figure 1. Health risks for personal safety and suicide related injuries, students in grades 9-12, Rhode Island, 1997-2007.



		1997	1999	2001	2003	2005	2007
S	Physical fighting	35.2	No data	31.4	27.6	28.4	26.3
S	Weapon carrying	17.7	No data	11.3	12.3	12.4	12.0
S	Hurt by Friend	No data	No data	9.2	8.1	9.7	14.0
S	Forced Sex	No data	No data	7.7	6.3	6.4	10.1

Note: An "S" next to the line graph legend box denotes a statistically significant linear change.

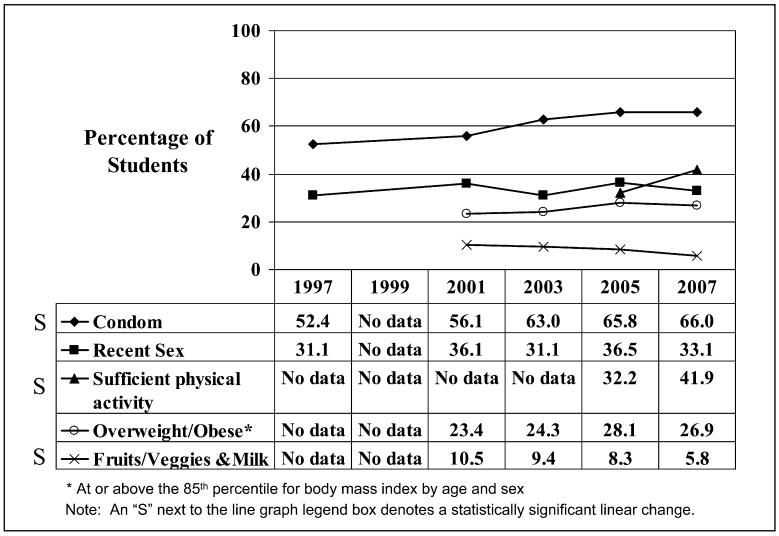
Figure 2. Health risks for violence related injuries, students in grades 9-12, Rhode Island, 1997-2007.



		1997	1999	2001	2003	2005	2007
S	Current alcohol	52.2	No data	50.3	44.5	42.7	42.9
S	Current cigarettes	35.4	No data	24.8	19.3	15.9	15.1
S	Current marijuana	28.7	No data	33.2	27.6	25.0	23.2

Note: An "S" next to the line graph legend box denotes a statistically significant linear change.

Figure 3. Health risks for substance abuse, students in grades 9-12, Rhode Island, 1997-2007.



		1997	1999	2001	2003	2005	2007
S	Condom	52.4	No data	56.1	63.0	65.8	66.0
	Recent Sex	31.1	No data	36.1	31.1	36.5	33.1
S	Sufficient physical activity	No data	No data	No data	No data	32.2	41.9
	Overweight/Obese*	No data	No data	23.4	24.3	28.1	26.9
S	Fruits/Veggies &Milk	No data	No data	10.5	9.4	8.3	5.8

* At or above the 85th percentile for body mass index by age and sex
Note: An "S" next to the line graph legend box denotes a statistically significant linear change.

Figure 4. Health risks for sexual behavior, weight, nutrition, and physical activity, students in grades 9-12, Rhode Island, 1997-2007.

Among violence-related behaviors (Figure 2), there were significant improvements between 1997 and 2007 in physical fighting in the past year (35% to 26%) and weapon carrying in the past month (17% to 12%). However, there was a significant worsening trend between 2001 and 2007 in being hurt (hit or slapped) by a girlfriend or boyfriend in the past year (9% to 14%) and forced sexual intercourse ever (8% to 10%). Figure 3 shows significant improvements between 1997 and 2007 in current (past month) alcohol (52% to 43%), cigarette (35% to 15%), and marijuana use (29% to 23%).

Recent sexual intercourse (past 3 months) remained unchanged at about one third of students from 1997-2007. (Figure 4) In contrast, more students wore a condom during last sexual intercourse (52% to 66%). The trend from 2001 to 2007 for overweight or obese students was relatively stable (23% to 27%).

From 2001-2007 fewer students consumed an adequate amount of fruits, vegetables, and milk (11% to 6%). The CDC standard is 5+ servings of fruits and vegetables per day and 3+ glasses of milk per day. However, the percentage for sufficient physical activity (60+ minutes per day for 5+ days per week) increased significantly from 2005-2007 (32% to 42%).

Discussion

There were improving trends between 1997 and 2007 among public high school students in seatbelt and bicycle helmet use; riding in a vehicle with a driver who has been drinking; physical fighting; weapon carrying; current alcohol, cigarette, and marijuana use; condom use; and physical activity. However, the 2007 data show 4 in 5 students who ride a bicycle still do not wear a helmet; 3 in 5 have insufficient physical activity; 2 in 5 are current alcohol drinkers; 1 in 3 have had recent sex; and 1 in 4 ride in a vehicle with an impaired driver, have been in a physical fight, or are overweight or obese, respectively.

The YRBS also highlights significant worsening trends in nutrition: only 6% of students in 2007 consumed an adequate amount of both fruits/vegetables and milk. Even more distressing, individual proportions for dating violence and forced sexual intercourse increased to where more than 1 in 10 students are victims. Furthermore, can society ever consider any level of attempted suicide among adolescents to be acceptable?

The YRBS is a comprehensive tool that state and community organizations can utilize to provide data for needs assessment and for planning and evaluating health promotion programs for youth. The survey is also a major source for monitoring objectives in *Healthy Rhode Islanders 2010*,[4] the state-specific version of the national *Healthy People 2010.* These objectives pertain to physical activity, overweight and obesity, tobacco use, substance abuse, and sexual behavior. *Healthy Rhode Islanders 2010* serves as a guide for targeting programs and a benchmark for assessing progress in youth-oriented efforts.

Disclosure of Financial Interests

The authors have no financial interests to disclose.

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Donald K. Perry, MPA, is the Manager for School-Based Health Surveys, Center for Health Data and Analysis, and Coordinator for Rhode Island's YRBS, Rhode Island Department of Health.

Yongwen Jiang, PhD, is an epidemiologist, Center for Health Data and Analysis, Rhode Island Department of Health.

still

Sarah Elizabeth Wakeman

on a shelf it sits
wrapped there in grays and blues
with edges taped tight
i turn my back, avert my eyes
i laugh and move and live
and stretch my mouth with smiles

but still it sits.

like a shadow it lingers, attached
but separate, a dark silhouette affixed to my seams
its presence hovers, magnetic
from afar it pulls, up close repels
an irreconcilable force
now and then i think i almost forget

but still it sits.

last week i took it down
and held it between two cold hands
careful and deliberate i began to examine
turning it over, touching its contours
the weight of sorrow heavy in my palms
seal unbroken, i reached high and shoved it back

and still it sits.

This poem was written about the author's struggle to deal with grief after her father's death.

CORRESPONDENCE:
Sarah Elizabeth Wakeman
e-mail: sarah.e.wakeman@gmail.com

Point of View

Smoking In Theatrical Productions

Herbert Rakatansky, MD, FACP, FACG

The campaign to decrease smoking is one of the most successful public health efforts supported by the medical profession. Smoking now is banned in virtually all public places in this country. There is, however, one exception where smoking continues in public.

Recently I attended play and an opera. In both, the performers smoked on stage. The opera was an early, obscure, seldom performed Wagner work. As such it attracted an international audience to the venue in Cooperstown, NY. Perhaps those audience members from countries where smoking is common found nothing strange. I found the multiple frequently lit cigarettes surprising. The play was here in Providence; and multiple characters smoked on stage.

The effort to ban smoking has been successful due to the recognized harm both to smokers themselves and to non-smokers forced to inhale the smoke. But there are even more reasons for actors not to smoke. Actors and singers depend on a healthy larynx for their careers. Smoke is an irritant and directly toxic to the larynx. Why an actor/singer would risk such damage or why a director would ask them to assume such a risk is unknown to me.

I understand very well that the director and performers must do what is needed to achieve their artistic vision unimpeded by outside influence. But smoking on stage is so unhealthy that one might question whether it falls outside the limits of artistic license. In the case of the opera, the characters were smoking to accentuate their "dissolution." In the play, the characters were smoking to appear "cool." I believe, however, that the talented artists involved in these productions have sufficient skills and technical expertise to portray their characters as dissolute or cool without smoking. We have been conditioned by the movies from the 40s and 50s to link smoking to many emotions, such as feeling romantic, "cool", sinister and even "manly." But remember that John Wayne died of lung cancer. Times change and we need not adhere to previous imagery when doing so is dangerous.

One of the objectives of the campaign against smoking is to prevent children from starting. Advertising directed at children and the sale of cigarettes to children is illegal. The AMA Alliance, the volunteer arm of the American Medical Association, estimates "3,900 children ages 12-17 try their first cigarette every day" in the US. The Alliance has suggested that movies, which contain "gratuitous" or prominent smoking, be rated R

so children will be less likely to see them. The movie "Incredible Hulk" has been targeted recently as an egregious example of such a movie. While children are not likely to flock to see a rare Wagner opera, many would have seen the theatrical production, as there were educational performances for students. Should parents have been warned that there was a significant amount of smoking, portrayed as desirable? Should parents have been asked for permission to allow their children to see the play? Most children seem to put a lot of time and effort into being "cool."

Theaters routinely warn audiences when a strobe light is to be used since it may (extremely rarely) cause a seizure in some people prone to them. Movies are rated based on language or behavior that is deemed unacceptable for children. We seem to agree that explicit sexual content and graphic violence are valid criteria to use to restrict access by children. The portrayal of smoking as desirable is no less harmful to children. Smoking is dangerous, with no redeeming individual or social value. Smoking benefits only the tobacco industry.

Censorship of artistic expression is neither desirable nor acceptable and generally not legal in our society. Autonomy to control our lives and actions within the limits of the law is one of our core values. We have learned in many situations, often with difficulty, that autonomy cannot be wisely exercised without adequate facts upon which to base our decisions. There should be warnings to the audience that smoking will occur on stage. Perhaps theater productions should have ratings? Should an independent body monitor the availability of information available to the public about on-stage smoking?

In our "information age" the public should have easy access to information about on stage smoking during performances so that we may make informed decisions about whether we wish to partake or allow our children to partake in the artistic endeavor.

Herbert Rakatansky, MD, FACP, FACG, is Clinical Professor of Medicine Emeritus, The Warren Alpert Medical School of Brown University, and Chair, RIMS Physician Health Committee.

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CORRESPONDENCE:
Herbert Rakatansky, MD, FACP, FACG
e-mail: herbrak1@cox.net

The views expressed are those of the author, not of the Medical Society.

2008 Tar Wars® Rhode Island Statewide Poster Contest

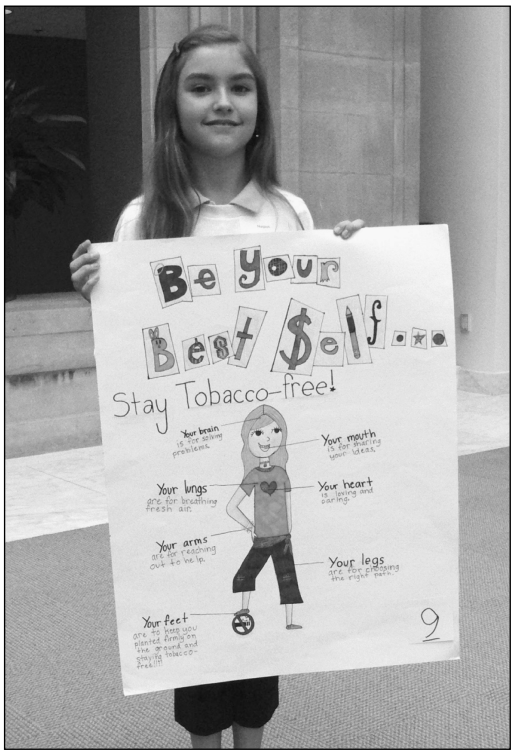
Held annually in Rhode Island since 1994, the Tar Wars® poster contest brings together fifth-grade students to compete for an all-expenses paid trip to Washington, DC to participate in the National Tar Wars® poster competition. Sponsors for this year's event were Newport Hospital, the Rhode Island Academy of Family Physicians, the Rhode Island Chapter of the American Academy of Pediatrics, and the Rhode Island Medical Society.

Judges for the 2008 Tar Wars® Rhode Island Statewide Poster Contest included **Dr. Sarah Fessler**, President of the Rhode Island Academy of Family Physicians; **Dr. Patricia Flanagan**, Board Member of the Rhode Island Chapter of the American Academy of Pediatrics; **Barbara Morse Silva**, Channel 10 News Health Reporter; **Dr. Nick Tsiongas**, President of the Rhode Island Medical Society; and **Dr. Terry McWilliams**, Vice President of Medical Affairs at Newport Hospital.

The winner of the 2008 Tar Wars® Rhode Island Statewide Poster Contest was Margaux Fontaine from The Community School in Cumberland, RI. Margaux, along with her mother, father, and sister, traveled to Washington, DC, in July to represent Rhode Island in the 20th Annual National Tar Wars™ Poster Contest. Margaux won 5th placed honors in the national event.

The second-place winner of the 2008 Tar Wars® Rhode Island poster contest was Robert J. Esposito, III, from R. C. LaPerche School in Smithfield. Anna Sroczynski, from St. Philomena School in Portsmouth, won third place.

Developed by the Academy of Family Physicians in 1988, Tar Wars® teaches critical thinking about tobacco advertising. Each year, roughly 70 RIMS member physicians volunteer their time to go into as many as 51 elementary schools throughout Rhode Island. Physician volunteers are needed for RIMS' 2009 Tar Wars® program. Please contact Catherine Norton at RIMS for more information. Phone: (401) 528-3286. e-mail: cnorton@rimed.org.



Business, Gifts and Boundaries In the Physician Patient Relationship

Robert S. Crausman, MD, and Jeannine Jeha

Neither a borrower nor a lender be;
For loan oft loses both itself and friend,

– Lord Polonius to his son Laertes.
Hamlet Act 1 Scene 2

A senior community-based physician practicing in Rhode Island established a physician-patient relationship with a wealthy patient. Over the course of several years, the patient, who happened to be both his neighbor and insurance agent, lent $177,000 to this physician. These loans were documented as part of the medical record. As the patient's health declined, the physician provided home care, at which point the patient's son became more involved in his father's financial affairs. The son subsequently became aware of the outstanding loan to the physician. The son made several attempts to collect payment from the physician; however, the physician was unable or unwilling to repay the debt. Despite the lack of repayment, both patient and family were pleased with the medical care provided and happy for the physician's willingness to provide home visits which allowed the patient to remain in the community until his passing. The unpaid loans, however, were a lingering source of concern.

Sometime after the patient's death, a complaint was filed with The Board of Medical Licensure and Discipline.

The Board investigated and substantiated the complaint through interviews with the physician, son, and review of the medical record. In its review, the Board recognized the son's dilemma in wanting to pursue collection of the overdue debt, but fearing that in doing so he would jeopardize his father's care and ability to remain in his home. The Board found that the physician's behavior constituted unprofessional conduct in the practice of medicine.

In view of the physician's considerable volunteer teaching and community work, the Board limited the sanction to a year of probation and required the completion of a personalized ethics program.

Ideally, the physician-patient relationship is a binding social agreement in which a physician agrees to place the patient's welfare ahead of his own self-interest.[1] Physicians are granted special access into their patients' lives: patients undress physically and emotionally to reveal highly personal and private information with the expectation that it is to be used to benefit their own health. This vulnerability makes them particularly susceptible to manipulation and potential abuse. Ethically, while the physician is expected to honor patient autonomy, it is the physician who is viewed to be in the "power" position. Patients are entitled to a relationship with their physician safe from financial manipulation.

This case also raises several concerns akin to those that arise around gifts to physicians. Some gifts, typically of token value, represent appropriate expressions of appreciation from patients and can act to enhance the physician-patient relationship.[2] Others have the potential by either intent or unintended consequence to influence care or to secure preferential treatment and therefore may compromise the physician's judgment; a physician should not accept such gifts.

Similarly, physicians are discouraged from entering into business arrangements with patients that may either negatively impact upon or take advantage of the physician-patient relationship.

In this case the patient's declining health led to the introduction of a 'key third party' – the patient's son – into the relationship. As a key third party, the son has legitimate standing in the physician-patient relationship. Physicians should consider a key third party as an extension of the patient with whom all ethical boundaries apply. Here the son's dilemma was also the patient's and physician's. The son had a fiduciary responsibility to the father to assure the payment of the physician's debt. Simultaneously, he had an obligation to assure appropriate medical care and to honor his father's wishes to remain in the home. The physician's willingness to make medical home visits was a critical factor that enabled the father to remain home near the end of life. Thus, the son had the understandable concern that taking action to force the physician to pay the overdue debt might adversely affect his father's care. Specifically, although the physician was never accused of suggesting a linkage, the son feared that the physician would stop making home visits.

Stressing the importance of integrity in the physician-patient relationship can help physicians better recognize and maintain appropriate professional boundaries. One reasonable criterion to apply where professional boundaries are concerned would be whether the physician would be comfortable if the business relationship were known to colleagues or the public.[2]

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Robert S. Crausman, MD, MMS, is Chief Administrative Officer, RI Board of Medical Licensure and Discipline.

Jeannine Jeha, a student at Northeastern University, was an intern at the RI Department of Health.

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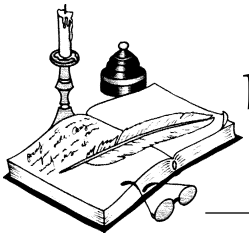
Correspondence:

Robert S. Crausman MD MMS
Chief Administrative Officer
RI Board of Medical Licensure and Discipline
3 Capitol Hill #205, Providence RI 02908
Phone: (401) 222-7888
e-mail: RSCrausman@aol.com



Physician's Lexicon

The Apocalyptic Prefix

The Greeks, it has been said, have a word for it. Actually, they had countless words expanded yet further by the artful employment of many meaningful prefixes and suffixes. The standard English-language medical dictionary, for example, lists 106 technical words beginning with the simple prefix, *apo-* , meaning away from, off, next to, or asunder [as in apomorphine, apoenzyme, apoferritin or apocleisis]. Actually, not all of these 106 medical terms beginning with the letters, *apo* are intended to be examples of the *apo-* prefix. A technical term such as apodia [think of it rather as a-podia than apo-dia] contains the Greek privative prefix, *a-*, [meaning not] attached to the basic root *-podia* and thus producing a word signifying a creature without feet. Other "false" *apo* words include such terms as apolitical or apollonian.

The non-medical employment of the *apo-* prefix includes the English term, apology, derived from the Latin, *apologia* and earlier from the Greek *logos*, meaning speech. Thus an apologue originally defined a moral truth or fable, an explanation often couched in parallel metaphors; and then, gradually the word defined either an explanation or justification for having caused injury; or sometimes, even a vindication for such events. An apostasy, representing a departure from one's doctrine or religion, is from the Greek root meaning stasis or standing and the prefix, *apo-* and thus signifying a standing apart, a departure from a formerly held credo or even a heresy [also from the Greek, meaning an alternate doctrine]. It must be distinguished, however, from words such as apostolic or apostle.

The word, apostrophe, joins the prefix, *apo-,* with the Greek word, *strephein*, meaning to turn or to twist, and through a succession of meanings [including the turning movements of the Greek chorus on the stage], to indicate, currently, a punctuation sign to signify an omitted letter. The word also describes an aside, or digression, in a formal speech. An apostrophe is also used to denote the possessive sense [eg., Zeus's daughter]. The word, apocalypse, literally to uncover or to disclose, has come to signify, ecclesiastically, a revelation.

The medical use of *apo-* includes apoplexy [literally, to strike aside or asunder], apothecary [literally, away from the storehouse] and aponeurosis [from an older meaning of neuron as a sinew].

– Stanley M. Aronson, MD

Rhode Island Department of Health
David Gifford, MD, MPH
Director of Health

Vital Statistics

Edited by Colleen Fontana, State Registrar

Rhode Island Monthly Vital Statistics Report Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	November 2007	12 Months Ending with November 2007		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	191	2,716	253.9	3,687.0
Malignant Neoplasms	211	2,277	212.9	5,962.5
Cerebrovascular Diseases	24	383	35.8	642.0
Injuries (Accidents/Suicide/Homicde)	31	515	48.1	8,076.0
COPD	36	423	39.5	322.5

Vital Events	Reporting Period		
	May 2008	12 Months Ending with May 2008	
	Number	Number	Rates
Live Births	956	12,827	12.0*
Deaths	778	10,032	9.4*
Infant Deaths	(9)	(86)	6.7#
Neonatal Deaths	(9)	(64)	5.0#
Marriages	636	6,802	6.4*
Divorces	178	2,955	2.8*
Induced Terminations	401	5,045	393.3#
Spontaneous Fetal Deaths	49	835	65.1#
Under 20 weeks gestation	(45)	(761)	59.3#
20+ weeks gestation	(4)	(74)	5.8#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,067,610

(c) Years of Potential Life Lost (YPLL)

Note: *Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.*

* Rates per 1,000 estimated population

\# Rates per 1,000 live births

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Ninety Years Ago, November 1918

From October 1918 through December 1919, because of World War I, the Rhode Island Medical Society suspended publication of the Journal. The Society's business manager and 2 members of the Editorial Staff had gone into service. "The faithful guard, who assumed extra duties at home that others might go to the front, found that the publication of the Medical Journal would be the straw which would eventually break the camel's back. Consequently they wisely decided not to attempt it."

Fifty Years Ago, November 1958

In "Bladder Neck Obstruction in Children," Lt. Edward H, Ray, Jr, MC USNR, Chief of Urological Service, US Naval Hospital, Newport, discussed the pathology, incidence, symptoms, diagnosis and treatment. "Any abnormality of the voiding pattern or any history of a urinary tract infection in a child should arouse suspicion that obstructive uropathy may exist."

Herman Kabat, MD, and Abraham Saltzman, MD, submitted "Electromyography – Aid to Diagnosis of Amyotrophic Lateral Sclerosis and Motor Root Compression Syndromes with [3] Case Reports." The authors concluded: "Electromyography may show fibrillation in all extremities in amyotrophic lateral sclerosis, even in the absence of muscular atrophy."

F.G. Ruest, MD, Director, Division of Tuberculosis Control, Rhode Island Department of Health, and Jean C. MacCorison, Executive Director, RI Tuberculosis and Health Association, reported on "Non-Hospitalized Tuberculous Patients in RI," a study undertaken with the US Public Health Service, the RI Department of TB Control, and the RI TB and Health Association. Of 257 patients who met the study criteria, 123 were "active and probably active;" 26 were "presumably active;" 108 were "other than active with drugs prescribed." One-third of active cases were under no medical supervision; 53% of active and presumably active cases had had no bacteriological report in the preceding 6 months. Standard regulations called for physicians to make the diagnosis, then report patients to a public health nurse, who would arrange to visit the patient. Forty percent of patients had not been referred to the nurse. "Only one-third of the active and presumably active patients at home were living under conditions conducive to adequate care of the patient and protection of his family and the public." The Report recommended: establish treatment facilities in outpatient departments of community hospitals for patients who refuse hospitalization and/or cannot pay for drug therapy; x-ray adult contacts of patients routinely every 6 months; encourage every newly diagnosed patient to go into the hospital for a brief work-up; increase use of the intradermal tuberculin test as a screening procedure.

An Editorial praised the Providence Rescue Squads, first established in 1943. The first year, the public called the rescue squad 254 times; in 1956, the public made 3,638 calls.

A second Editorial urged polio vaccinations. Of the Rhode Island population younger than age 40, 53% had not had the basic 3 injections; more than a third had had no vaccine at all. The first 9 months of 1958, the state had 1815 cases of polio, 258 more than the same period in 1957.

Twenty-Five Years Ago, November 1983

Wendy J. Smith, managing editor, contributed "The Nicotine Fix: A Personal Perspective." She traced the rise of the industry to James Buchanan Duke, "an impoverished former Confederate soldier [who] refined a method for the mass production of cigarettes in the 1880s." (He didn't smoke.) By 1888 Duke was selling 740 million cigarettes annually; in 1890 Duke formed the American Tobacco Company; in 1911 trust-busting legislation divided American Tobacco into 4 companies. In 1980 Americans smoked more than 4 billion cigarettes annually. In 1964 the US Surgeon General reported on the harmful effects: the mortality rate for smokers was 70% higher than for non-smokers. The author recounted her "failure to kick the habit." She argued that the key to success of anti-smoking campaigns was to "prevent adolescents from smoking that first cigarette."

William Bennett, MD, Editor of the Harvard Medical School Health Letter, contributed "The Nicotine Fix" (copyright-Harvard Magazine): "The industry is based on the principle of selling perhaps the most addicting of substances to minors."

William D. Torres, MD, and Leonard J. Triedman, MD, in "Computed Tomography in the Management of Head and Neck Cancers," posited that "New applications were expected to play an invaluable role in the early detection, management and follow-up of such tumors."

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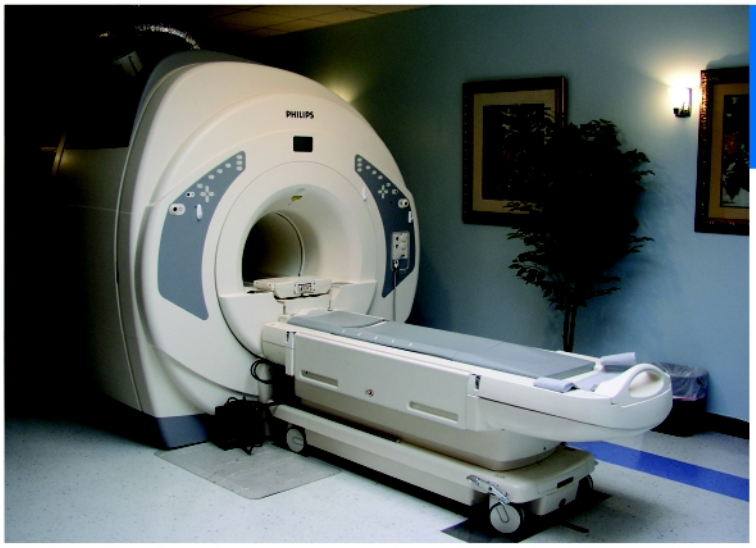

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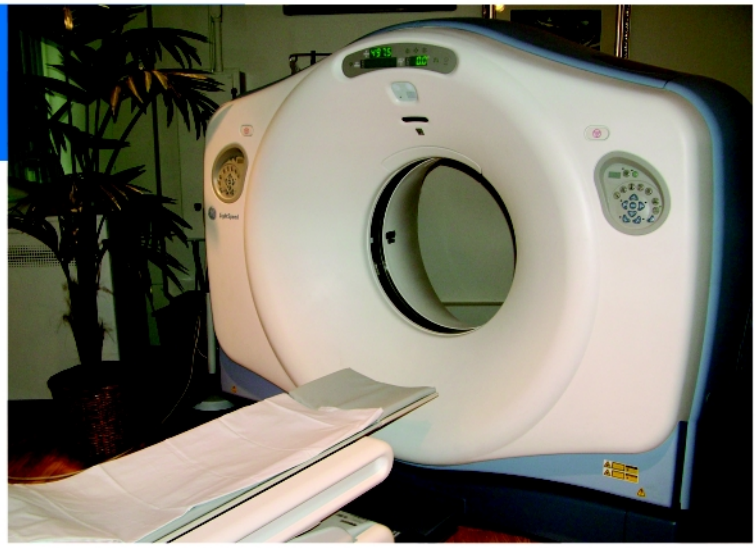

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It's Good to Have Endorsements in an Election Year

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